NERVE CONDUCTION ABNORMALITIES AND BRAINSTEM AUDITORY EVOKED POTENTIALS IN TYPE 2 DIABETES MELLITUS

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CERTIFICATE

This is to certify that this Dissertation entitled **"EVALUATION OF NERVE CONDUCTION ABNORMALITIES AND BRAINSTEM AUDITORY EVOKED POTENTIALS IN TYPE 2 DIABETES MELLITUS**" by the candidate **Dr. K.KANNAN** for **M.D Physiology** is a bonafide record of the research done by him during the period of study (2008 - 2011) in the Institute of Physiology and Experimental Medicine, Madras Medical College, Chennai – 600 003.

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INDEX

ABBREVATIONS

BAEP	–	BRAINSTEM AUDITORY EVOKED POTENTIAL.
CMAP	–	COMPOUND MUSCLE ACTION POTENTIAL.
CNS	–	CENTRAL NERVOUS SYSTEM.
DM	–	DIABETES MELLITUS.
DN	–	DIABETIC NEUROPATHY
MODY	–	MATURITY ONSET DIABETES OF THE YOUNG
NCV	–	NERVE CONDUCTION VELOCITY.

INTRODUCTION

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycaemia. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and life-style choices. Depending on the aetiology of the DM, factors contributing to hyperglycaemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production[1]. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. DM is the leading cause of end-stage renal disease (ESRD), nontraumatic lower extremity amputations, and adult blindness. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.

It is estimated that the global number of adults suffering from any form of diabetes will reach 285 million in 2010 and further increase to 439 million in 2030, most of them non insulin dependent diabetes mellitus cases [2,3]. Globally, type 2 diabetes mellitus has become one of the most important chronic public health problems[4] .

BROAD CLASSIFICATION OF DIABETES MELLITUS

1. Type 1 diabetes also called as insulin dependent DM (IDDM) is caused by lack of insulin secretion.

2. Type 2 diabetes also called Non insulin dependent DM (NIDDM) is caused by decreased sensitivity of target tissues to the metabolic effect of insulin.

Etiologic Classification of Diabetes Mellitus [1]

I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)

   A. Immune-mediated

   B. Idiopathic

II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)

III. Other specific types of diabetes

   A. Genetic defects of β-cell function characterized by mutations in:

      1. Hepatocyte nuclear transcription factor (HNF) 4α (MODY 1)
      2. Glucokinase (MODY 2)
      3. HNF-1α (MODY 3)
      4. Insulin promoter factor (IPF) 1 (MODY 4)
      5. HNF-1β (MODY 5)
      6. NeuroD1 (MODY 6)
      7. Mitochondrial DNA
      8. Proinsulin or insulin conversion

B. Genetic defects in insulin action:

1. Type A insulin resistance

2. Leprechaunism

3. Rabson-Mendenhall syndrome

4. Lipodystrophy syndromes

C. Diseases of the exocrine pancreas—pancreatitis, pancreatectomy, neoplasia, cystic fibrosis, hemochromatosis, fibrocalculous pancreatopathy.

D. Endocrinopathies-acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism, somatostatinoma, aldosteronoma.

E. Drug- or chemical-induced—Vacor, pentamidine, nicotinic acid,glucocorticoids, thyroid hormone, diazoxide, β-adrenergic agonists,Thiazides, phenytoin, α-interferon, protease inhibitors, clozapine,Beta blockers.

F. Infections—congenital rubella, cytomegalovirus, coxsackie.

G. Uncommon forms of immune-mediated diabetes—"stiff-man" syndrome, anti-insulin receptor antibodies.

H. Other genetic syndromes sometimes associated with diabetes—Down's syndrome, Klinefelter's syndrome, Turner's syndrome, Wolfram's syndrome, Friedreich's ataxia, Huntington's chorea, Laurence-Moon-Biedl syndrome, myotonic dystrophy, porphyria, Prader-Willi syndrome.

IV. Gestational diabetes mellitus.

CHRONIC COMPLICATIONS OF DM

The chronic complications of DM affect many organ systems and are responsible for the majority of morbidity and mortality associated with the disease. Chronic complications can be divided into vascular and nonvascular complications[1.]

Chronic Complications of Diabetes Mellitus[1]

Microvascular

- Eye disease.
- Retinopathy (nonproliferative / proliferative).
- Macular edema.
- Neuropathy.
- Sensory and motor (mono- and polyneuropathy).
- Autonomic.
- Nephropathy.

Macrovascular

- Coronary artery disease.
- Peripheral vascular disease.
- Cerebrovascular disease.

Other

- Gastrointestinal (gastroparesis, diarrhea).
- Genitourinary (uropathy/sexual dysfunction).
- Dermatologic.
- Infectious.
- Cataracts.
- Glaucoma.

The risk of chronic complications increases as a function of the duration of disease they usually become apparent in the second decade of hyperglycaemia. Since type2 DM often has a long asymptomatic period of hyperglycaemia, many individuals with type 2 DM have complications at the time of diagnosis[1]. Chronic complications are the major outcome of type 2 diabetes mellitus progress, which reduce the quality of life of patients, incur heavy burdens to the health care system, and increase diabetic mortality[5]

MECHANISMS OF COMPLICATIONS[1]

The exact mechanism(s) by which diabetes leads to such diverse cellular and organ dysfunction is unknown. Four prominent theories, which are not mutually exclusive, have been proposed to explain how hyperglycaemia might lead to the chronic complications of DM.

Advanced Glycosylation End Products (Ages) Theory

One theory is that increased intracellular glucose leads to the formation of advanced glycosylation end products (AGEs) via the

nonenzymatic glycosylation of intra and extracellular proteins. Nonenzymatic glycosylation results from the interaction of glucose with aminogroups on proteins. AGEs have been shown to cross-link proteins (e.g., collagen, extracellular matrix proteins), accelerate atherosclerosis, promote glomerular dysfunction, reduce nitric oxide synthesis, induce endothelial dysfunction, and alter extracellular matrix composition and structure. The serum level of AGEs correlates with the level of glycaemia, and these products accumulate as glomerular filtration rate declines.

Sorbitol Pathway Theory

A second theory is based on the observation that hyperglycaemia increases glucose metabolism via the sorbitol pathway. Intracellular glucose is predominantly metabolized by phosphorylation and subsequent glycolysis, but when increased, some glucose is converted to sorbitol by the enzyme aldose reductase. Increased sorbitol concentration alters redox potential, increases cellular osmolality, generates reactive oxygen species, and likely leads to other types of cellular dysfunction. However, testing of this theory in humans, using aldose reductase inhibitors, has not demonstrated significant beneficial effects on clinical endpoints of retinopathy, neuropathy, or nephropathy.

A third hypothesis proposes that hyperglycaemia increases the formation of diacylglycerol leading to activation of protein kinase C (PKC). Among other actions, PKC alters the transcription of genes for fibronectin, type IV collagen, contractile proteins, and extracellular matrix proteins in endothelial cells and neurons.

A fourth theory proposes that hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, a substrate for O-linked glycosylation and proteoglycan production.The hexosamine pathway may alter function by glycosylation of proteins such as endothelial nitric oxide synthase or by changes in gene expression of transforming growth factor β(TGF-β) or plasminogen activator inhibitor-1 (PAI-1).

DIABETES MELLITUS AND PERIPHERAL NERVOUS SYSTEM

Peripheral nervous system disorders are one of the more frequent long-term complications of diabetes mellitus. The clinical features, epidemiology and pathophysiology of peripheral diabetic neuropathy have been studied extensively. Diabetic neuropathy (DN) occurs in approximately 50% of individuals with long-standing type 1 and type 2 DM. It may manifest as polyneuropathy, mononeuropathy, and/or autonomic neuropathy. As with other complications of DM, the neuropathy correlates with the duration of diabetes; both myelinated and unmyelinated nerve fibers are lost[1].

DN is not a single entity but a number of different syndromes ranging from subclinical to clinical manifestation depending on the classes of nerve fibres involved. The main groups of neurological disturbance in DM include [6].

1) Subclinical neuropathy, determined by abnormalities in electro diagnostic and quantitative sensory testing.

2) Diffuse clinical neuropathy and distal symmetric sensorimotor and autonomic syndromes.

3) Focal syndromes.

The broad diversity of neurologic complications in patients with DM can be considered to consist of two distinct types. In one form the symptoms and signs are transient, in the other they progress steadily. The transient category includes acute painful neuropathies, mononeuropathies and radiculopathies. The progressive type comprises sensorimotor polyneuropathies with or without autonomic symptoms and signs[7].

The simplest and most widely used classification was initially proposed by Thomas[8]. This approach divides the diabetic neuropathies into diffuse, generalized or symmetrical polyneuropathies and focal neuropathies. A modification of this neuropathy is shown here[9].

A. SYMMETRIC NEUROPATHIES

1. Distal symmetrical sensorimotor polyneuropathy.

2. Autonomic neuropathy.

3. Acute painful neuropathy.

4. Hyperglycemic neuropathy.

5. Treatment induced neuropathy.

6. Symmetrical proximal lower extremity neuropathy.

B. FOCAL AND MULTIFOCAL NEUROPATHY

1. Cranial neuropathy.

2. Thoraco abdominal neuropathy.

3. Focal limb neuropathy.

4. Diabetic amyotrophy.

DIABETES AND CENTRAL NERVOUS SYSTEM

The involvement of central nervous system (CNS) in DM is recent concept. Woltman and Wilder[10] concluded from pathological material that diabetic neuropathy is a disease of peripheral nerves and that degeneration in the CNS is unimportant. However, it is reasonable to ask whether such a ubiquitous metabolic derangement and diffuse angiopathy might involve any part of the nervous system. Recent studies[11] showed the involvement of brain parenchyma in patients with long standing diabetes mellitus.

The central nervous system could also be abnormal in diabetic patients[12,13,14]. De Jong[15] has pointed to clinical and pathological evidence that the brain parenchyma might be affected. Kent[16] has argued that diabetic patients show some neurological and psychological symptoms that might signify premature aging. The pathophysiology of central nervous system (CNS) abnormalities in DM is not well understood, probably many causes are responsible for the neural damage, including, chronic hyperglycaemia, hypoglycaemic episodes, blood-brain barrier dysfunction, angiopathy, and others[17,18,19.] In diabetic patients, deficits have been reported in neuropsychological, neuroradiological and neurophysiological

studies. Neuropsychological studies report deficits in cognitive functions, in particular learning and memory and complex information processing[20].Neuroradiological studies report modest cerebral atrophy and an increased occurrence of subcortical and brainstem lesions[21,22]. Neurophysiological studies of the CNS in diabetic patients have mostly involved measurements of evoked potential latencies. Increases in the latencies of evoked potentials of different modalities, including visual evoked potentials (VEPs), brainstem auditory evoked potentials (BAEPs) and somatosensory evoked potentials, have often been reported[23].

Neurophysiological alterations have also been described in animal models of diabetes, in particular in rats. Neurophysiological alterations have been reported in the CNS of diabetic rats[24,25,26,27] by various studies, but the course of development is incompletely documented.

REVIEW OF LITERATURE

HISTORY OF CLINICAL NEUROPHYSIOLOGY [28]

Carlo Metteucci, Professor of Physics in Pisa, Italy, investigated the localisation of electricity in a nerve muscle preparation and proposed the concept of electrophysiological based functioning of the nervous system.

In 1850, Helmholtz succeeded in measuring the conduction velocity of nerve in frog by mechanically recording the muscle twitch. Employing the same procedure, the conduction velocity of median nerve was found to be 61.0 ± 5.1 m/s and that of sensory nerve 60 m/s. The first report of nerve action potential in response to median and ulnar nerve stimulation was published in 1937 by Eicher. The modern techniques of sensory nerve conduction measurements were developed a decade later.

In 1942, James Goldseth at NorthWestern University in collaboration with James Fizell , developed a constant current stimulator. The investigation of war injuries by Herburt Jasper in Canada resulted in the development of monopolar needle electrode .Interaction between Jasper, Goldseth and Fizell paved the way for the development of clinically useful electromyography equipment which was introduced in 1948 by Goldseth.

In 1944, Harvey and Kuffer applied nerve conduction studies in patients with peripheral neuropathy. Hodes, Laravee and German in 1948 first calculated conduction velocity by stimulating nerve at different levels. Nerve stimulation techniques were used to study the effect of ischemia on

nerve excitability and it was shown that the rate of impulse propagation slowed in ischemic nerve.

In 1956, Simpson demonstrated slowing of nerve conduction in carpal tunnel syndrome and Lambert and Kaesar differentiated demyelinating from axonal neuropathy.

PREVALENCE OF DIABETIC NEUROPATHY

Diabetic neuropathy is the most common and troublesome complication of diabetes mellitus leading to great morbidity and resulting in a huge economic burden for diabetes care[29.] However, the progression of neuropathy can be reduced by early detection and intervention[30]

In a prospective study of over 4400 diabetic out patients, Pirart J[31] reported an overall 12% prevalence rate of diabetic neuropathy in patients with newly diagnosed diabetes and the incidence of neuropathy increased with the duration of diabetes and after 25 years of diabetes, over 50% of patients had DN[31]. In another study[32] it was reported prevalence of neuropathy was 5% in the 20 to 29 year old group and increased with age, reaching 44.2% in patients between 70 to 79 years of age.

Prevalence is typically higher if ascertainment is based on electrophysiological measurements, but lowers if it is based on subjective symptoms and physical findings only. The prevalence of neuropathy also increases with age and increasing duration of diabetes[9]. Diabetic patients have a 12 times higher risk of amputations when compared with non-diabetic subjects, due to diabetic neuropathy[33]. The presence of other

vascular complications such as peripheral vascular disease in diabetes increases the risk of diabetic foot complications[34.]

ROLE OF ELECTROPHYSIOLOGICAL STUDIES IN DIABETIC NEUROPATHY

Evaluation of neuropathy is generally undertaken by electrophysiological measurements[35] .According to San Antonio Conention of neuropathy the patient with diabetic neuropathy must have a sign or a symptom and an abnormal electrodiagnostic test[36]. Electrophysiological studies are more sensitive than clinical examinations as clinical examinations fail to offer quantitative results and the electrodiagnostic tests are the least variable non invasive measures of neuropathy.

Electrodiagnostic tests have widespread applications and are reliable, reproducible measures of peripheral nervous system function. They are objective measures that are relatively independent of patient effort or cooperation. Nerve Conduction Study (NCS) and needle Electromyography (EMG) are well accepted for the evaluation of DN [37,38]. They are sensitive measures, able to detect abnormalities in diabetic patients that may not be clinically apparent.

Electrophysiological measures of nerve function have been the mainstay of 'objective' assessment of neurological deficits in diabetic patients[39]. Some form of abnormality can be detected in the majority of patients. Symptoms do not necessarily correlate with the electrophysiological abnormalities [40]

Nerve conduction studies, primarily nerve conduction velocities are considered one of the most sensitive indices of the severity of neuropathy[41]. Nerve conduction tests are used to localize lesions and to describe the type and severity of the pathophysiologic process, including alterations in function that are not recognized clinically. Lehtinen JM et al[42] had reported that clinical diabetic neuropathy is not common at diagnosis of Type 2 diabetes but disturbances in peripheral and autonomic nerve function as noted by electrophysiological and cardiovascular reflex method are often present at that stage. In Type 2 diabetic patients decreased Nerve Conduction Velocity (NCV) is probably one of the earliest neuropathic abnormalities and is often present even at diagnosis. Thereafter, slowing of NCV generally progresses at a steady rate of approximately 1 m/s/year and it shows a correlation with the duration of diabetes.[43]

NERVE CONDUCTION STUDIES IN DIABETES

In a study done on diabetic patients, reduced sensory nerve action potential (SNAP) amplitude was observed in the medial nerve in 70% of the patients, in the ulnar in 69% and in the sural nerve in 22%. No correlation was found between metabolic indices and nerve conduction study parameters. High percentages of newly diagnosed DM patients show signs of neuropathy, and upper limb nerve sensory NCS seem to be more sensitive in detecting it than lower limb NCS [44].

In a study done on diabetics with and without neuropathy, the amplitude and nerve conduction velocity (NCV) were lowered in both groups, particularly in those with neuropathy. Estimation of conduction

velocity can be considered as more useful parameter than the measurement of amplitude in the diagnosis and evaluation of neuropathy in diabetics. Assessment of sensory nerve conduction in median nerve is a better indicator than that of ulnar nerve[45]

The independent risk factors for DN were female gender, height, age, weight, HbA1C and duration of diabetes. The only parameter linearly related to all these nerve conduction measurements was duration of diabetes, where increased duration was associated with longer latency, lower amplitudes and lower NCVs [46]. The attributes of NCS that are likely to be most useful are summated or averaged sensory nerve action potential amplitude and averaged motor NCV[47].

Biswas[48] observed deterioration of motor nerve function without sensory nerve dysfunction in fairly controlled type 2 diabetic subjects with shorter duration of diabetes.

Gregerson[49] found that motor conduction may get reduced in diabetes and positive correlation was demonstrated between neglected diabetes control and slowing of motor conduction velocity. Fagerberg et al[50] also demonstrated that motor conduction velocity decreases with duration of diabetes.

The recording of a nerve action potential of normal latency, amplitude, and wave form requires synchronous conduction in the large myelinated fibres[51]. In diabetic neuropathy, the sensory nerve potentials are characterized by reduced amplitude, a polyphasic shape and an increased latency of the initial peak. These alterations can also appear,

though to a lesser degree, when a careful clinical examination of the nervous system is negative[52]

BRAINSTEM AUDOTORY EVOKED POTENTIAL ABNORMALITIES IN DIABETES

Central diabetic neuropathy is a newer concept and it can be detected by simple and non-invasive methods. One of these methods is brainstem auditory evoked potentials (BAEP)[53,54] and interpretations of them. By this method, functional and autonomic pathologies from the acoustic nerve to the upper part of the brainstem can be demonstrated at an early stage[54]. Lesions on these levels result in changes in BAEP amplitudes and latencies. Evaluation of these changes might help to determine early subclinical injuries restricted to the afore mentioned regions [55].

Brainstem auditory evoked potentials in rats with streptozotocin-induced diabetes

Roberto Rubini et al[56] studied Brainstem auditory evoked potentials (BAEPs) in streptozotocin (STZ)induced -diabetic rats and age-matched controls at 3 and 5 months from induction of the pathology. The diabetic status of the animals was kept uncontrolled throughout the study. Body weight and glycosylated haemoglobin were markedly altered in the diabetic animals (− 42% and + 120% of control values, respectively). Neurophysiological results showed an increase in the latency of the major components of BAEPs; this increase was clearly time-dependent for the peripheral component (peak I). The central component (peak IV) was also significantly delayed. However, no significant impairment of the central conduction time was demonstrated by examining the interpeak I–IV

latency. In conclusion, BAEPs prove to be a useful non-invasive neurophysiological technique that may help unravel both the relative involvement of the central nervous systems in the course of diabetes mellitus, and the evolution of diabetic neuropathy.

Evaluation of Central Neuropathy in Type II Diabetes Mellitus by Multimodal Evoked Potentials

Hikmet Dolu et al[57] conducted various electrophysiological tests in 51 patients with type II DM and compared them with 30 age and sex matched healthy control subjects. Peripheral and cortical latencies of median and tibial somatosensory evoked potentials (SEP), bilateral I-III and I-V interpeak latencies (IPL) of brainstem auditory evoked potentials (BAEP), bilateral P100 latency of visual evoked potentials (VEP) and bilateral cortical latency and central motor conduction time of motor evoked potentials (MEP) were evaluated. They observed prolonged latencies suggestive of central neuropathy in DM type II. It has been shown that most of the electrophysiological parameters in patients with DM type II correlate with the duration of the disease, some of them with the age of the patient, and few of them with the onset of the disease and found out knowledge, there is no correlation between the electrophysiological parameters and the level of glycaemia or the degree of metabolic control. They concluded that central and peripheral neuropathies in DM are related to the duration of the disease and not to the degree of hyperglycaemia and metabolic control.

Auditory Brainstem Latencies In Type I (Insulin-Dependent) Diabetic Patients

Jukka Virtaniemi et al[58] studied auditory brainstem latencies in 53 type I diabetic patients and 42 randomly selected non diabetic control subjects, aged between 20 and 40 years. They found out that Wave V latencies were longer in diabetic patients when compared with those of control subjects at all repetition rates and concluded that delayed auditory brainstem latencies in type I diabetic patients are probably caused by the long duration of diabetes and the microvascular complications associated with it.

Brainstem auditory evoked potentials study in patients with Diabetes mellitus

Chi-Ren Huang et al[59] analysed the correlation between brainstem-auditory evoked potentials (BAEP) and nerve conduction (NC) studies in patients with diabetes mellitus (DM) and retrospectively reviewed the results from the subjects who received neurological screening test including BAEP and NC studies. A DM group and a control group were applied. The DM group was subdivided 4 subgroups including neuropathy, non-neuropathy, infarct and non-infarct. At the end of the study they concluded that Patients with DM have a prolongation in IPL I-III, especially in the neuropathy subgroup. This prolongation in IPL I-III would best be explained by acoustic neuropathy. The tibial motor, median sensory, and sural NC velocities correlated with the acoustic neuropathy in patients with DM.

Delayed Auditory Brainstem Responses in Diabetes Mellitus

M.W Donald et al[60] found that Diabetic patients have longer interpeak latencies in the brainstem auditory evoked responses than age-matched controls. The delay is not related to clinical hearing loss or blood glucose level at the time of testing. Since waves I and II are normal in latency, the conduction velocity of the eighth nerve is not involved. The delay occurs between waves II and V, which would reflect altered transmission times in auditory brainstem and midbrain structures, and suggests the presence of a central neuropathy in patients with diabetes.

The observed delay in central transmission time in diabetics may be related to the pathological observations like degeneration of the ganglion cells and nerve fibres of the cerebrum, brainstem, and cerebellum-severe enough histologically to justify the use of the term "encephalopathy"[11].

Olsson et al [61] and Reske-Nielsen et al [11] on the basis of detailed pathoanatomic studies concluded that brain involvement is common in longstanding diabetes.

Nerve conduction velocity and evoked potential latencies in streptozotocin diabetic rats

Biessels GJ et al [62] observed that, in streptozotocin (STZ) diabetic rats, deficits in cerebral function develop gradually in the course of months and there is a significant deficit in nerve conduction velocity and evoked potential latencies.

Kamal A et al [63] demonstrated learning deficits in experimentally induced diabetic rats develop in association with deficits in synaptic plasticity. In addition, deficits in impulse conduction velocity develop in the brain, as reflected in increased evoked potential latencies.

Masana Y et al[64] and Sima AA et al[65] found out that in diabetic rats there is a significant deficit in nerve conduction velocity and evoked potential latencies. They documented an increased interpeak latency III-V in the BAEP and VEP p1 latency found in diabetic rats

AIMS AND OBJECTIVES

1. To study the effects of the involvement of peripheral and central nervous system in non insulin dependent diabetic individuals by doing nerve conduction studies and brainstem auditory evoked potentials and comparing it with controls.

2. To assess whether the duration of the disease is related to the degree of damage to the nerve.

3. To compare the involvement of peripheral and central nervous system damage.

MATERIALS AND METHODS

The study was conducted during the year 2009 – 10 in the Institute of Physiology and Experimental Medicine, Madras Medical College, after getting permission from the Institutional Ethical Committee, Madras Medical College, Chennai.

Type 2 diabetes mellitus patients of both sexes in the age group between 35 and 55, were included in the study. They were selected from the Diabetology outpatient department, Government General Hospital, Chennai – 600 003. All the participants were informed about the study and procedure in their native language and a written consent was obtained from them. Age and sex matched healthy subjects were used as controls.

INCLUSION CRITERIA.

- Age group 35 – 55 years, of both gender.
- Type 2 Diabetic patients with or without symptoms of neuropathy.
- Both recently diagnosed and chronic diabetic patients.
- Patients on oral hypoglycemic agents or insulin or both.

EXCLUSION CRITERIA

- Hypertension.
- Smoking and alcoholism.
- History of head injury.
- Drug intake (ototoxic drugs).
- Ear surgery.

- External ear / middle ear pathologies.
- Conductive / mixed hearing loss.
- Patients with other metabolic abnormalities causing neuropathy.
- Patients on drugs leading to neuropathy.
- Patients with cochlear implant / cardiac pacemeaker.

MATERIALS

STUDY GROUP (Diabetics)

40 type 2 Diabetes mellitus patients in 35-55 years age group.

Subgroups

Group I - type 2 DM patients with duration of diabetes between 0-7 years.

Group II - type 2 DM patients with duration of diabetes between 7-15 years.

CONTROL GROUP

40 age and sex matched healthy controls. The following tests were conducted in the study and control group

1. Nerve conduction study of
   a. Median nerve of right upper limb – motor and sensory components.
   b. Tibial nerve (motor) of right lower limb.
2. Brain stem auditory evoked potentials.

   Both the tests are conducted using RMS – EMG MEDICARE SYSTEMS. (**Photograph 1)**

Photograph 1. RMS – EMG Recorders Medicare Systems

PRECAUTIONS

(1) The subject should be properly instructed and motivated to provide full cooperation.

(2) The subject should be fully relaxed.

(3) The room should be quiet and comfortable.

(4) The subject should be grounded properly

NERVE CONDUCTION STUDY

PRINCIPLES OF MOTOR NERVE CONDUCTION[28]

The motor nerve is stimulated at two points along its course. The pulse is adjusted to record a compound muscle action potential. Typically, the impulse is generated using a bipolar stimulator placed on the surface of the skin over the anatomic course of nerve being tested. The nerve is subjected to supramaximal stimulation keeping the cathode close to the active recording electrode. This prevents the hyperpolarisation effect of anode and anodal conduction block. The surface recording electrodes are used and placed in belly tendon montage, keeping the active electrode close to the motor point and reference to the tendon, ground electrode is placed between the stimulating and recording electrodes.

A biphasic action potential with initial negativity is recorded. Surface stimulation of healthy nerve requires a square wave pulse of 0.1 ms duration with an intensity of 5-40 ma (milliamperes). Filter setting for motor nerve conduction study is 5khz-10khz and sweep speed 2-5 ms/division.

The measurement for motor nerve conduction study include the following

1. Onset latency.

2. Amplitude of compound muscle action potential (CMAP).

3. Duration of compound muscle action potential.

3. Nerve conduction velocity.

ONSET LATENCY

The onset latency is the time in ms from the stimulus artefact to the first negative deflection of CMAP. It is a measure of conduction in the fastest conducting motor fibres. It also includes the neuromuscular transmission time and the propagation time along the muscle membrane which constitute the residual latency.

AMPLITUDE

The amplitude of CMAP is measured from baseline to the negative peak (base to peak) or between negative and positive peaks (peak to peak). The amplitude correlates with number of nerve fibres.

DURATION

The duration of CMAP is measured from the onset of response to the negative or positive peak or the final return of waveform to the baseline. Duration correlates with the density of small fibres.

MOTOR NERVE CONDUCTION VELOCITY

This is a measure of speed of impulse conduction. Motor nerve conduction velocity is calculated by measuring the distance between two points of stimulation in mm which is divided by the latency difference in millisecond. The nerve conduction velocity is expressed as m/sec (metre/second). Measurement of latency difference between the two points of stimulation eliminates the effect of residual latency.

$$\text{Conduction velocity} \quad \frac{D}{PL - DL}$$

PL----proximal latency in milliseconds (ms).

DL----distal latency in milliseconds (ms).

D----distance between proximal and distal stimulation in millimetres.

For accurate motor nerve conduction velocity measurement, the distance between two points of stimulation should be at least 10 cm. This reduces the error due to faulty measurement.

PRINCIPLES OF SENSORY NERVE CONDUCTION[28]

The sensory nerve conduction can be measured orthodromically or antidromically. In orthodromic conduction, a distal portion of the nerve e.g. digital nerve is stimulated and sensory nerve action potential (SNAP) is recorded at a proximal point along the nerve. In antidromic sensory nerve conduction, the nerve is stimulated at a proximal point and nerve action potential is recorded distally. For orthodromic conduction ,ring electrodes are preferred to stimulate the digital nerve, whereas surface

stimulating electrodes are commonly used for antidromic conduction.The recommended filter settings for sensory conduction is 10Hz-2KHz, sweep speed 1-2ms/division and gain 1-5μv/division. The signal enhancement with averaging is generally required for sensory conduction velocity. The signal enhancement with averaging is proportional to the square root of the number of trials.

Change in amplitude =square root of n.

n= no of trials, which is kept at 20.

EXPERIMENTAL PROCEDURE

NERVE CONDUCTION STUDY – MEDIAN NERVE

Motor and sensory components were tested.

MEDIAN NERVE (motor)

Recording electrode : close to the motor point of abductor pollicis brevis.

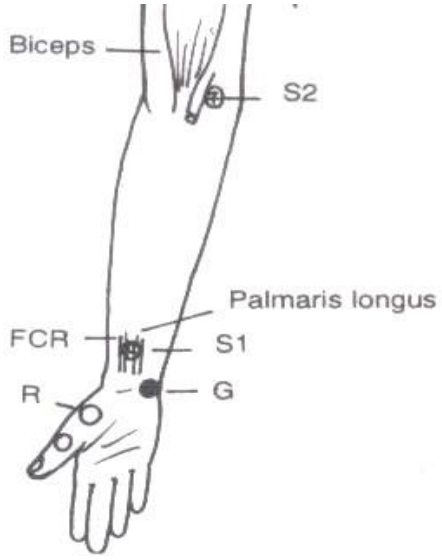
Reference electrode : 3 cm distal to 1st metacarpo phalangeal joint.

Stimulation 1 : at wrist 3 cm proximal to distal wrist crease.

Stimulation 2 : at elbow near the volar crease of brachial pulse.

Refer Fig: 1

Fig: 1. Electrode Placement for Motor Conduction of Median Nerve



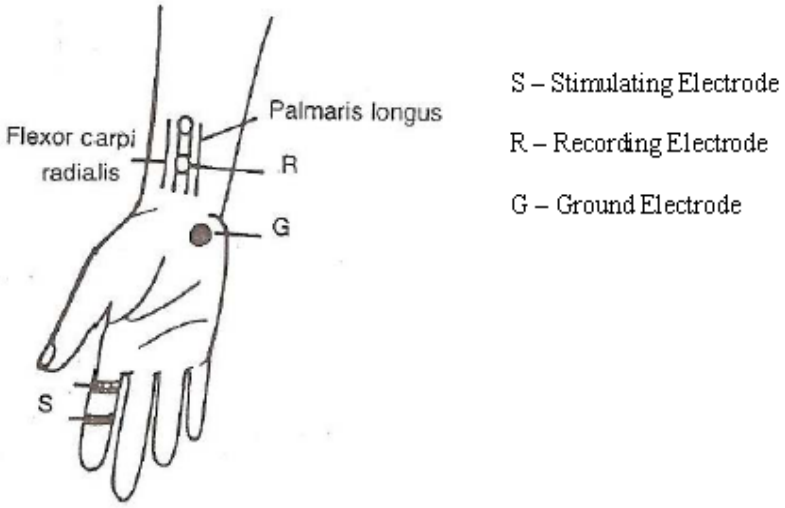
S1 – Stimulation at the wrist
S2 – Stimulation at the elbow
G – Ground
R – Reference

MEDIAN NERVE (sensory)

Recording electrode	:	proximal interphalangeal joint.
Reference electrode	:	distal interphalangeal joint.
Stimulation	:	wrist.

Refer Fig.2

Fig 2. Electrode placement for orthrodomic sensory conduction of median nerve.

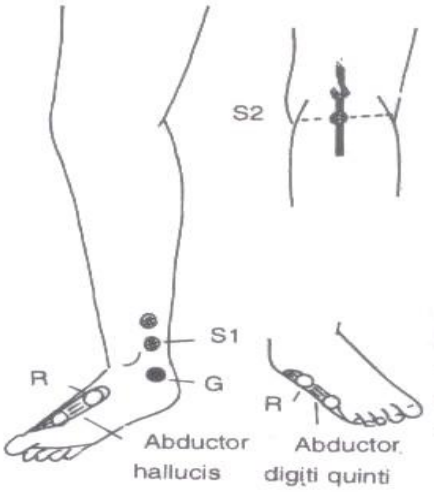


TIBIAL NERVE (motor)

Recording electrode	:	Abductor hallucis slightly below and anterior to navicular tuberosity
Reference electrode	:	5cm distal to the recording electrode.
Stimulation 1	:	behind and proximal to the medial malleolus.
Stimulation 2	:	in the popliteal fossa along the flexor crease of the knee slightly lateral to midline of the popliteal fossa

Refer fig 3

Fig: 3. Electrode Placement for Motor Conduction of tibial Nerve.



S1 – Stimulation near the medial malleolus
S2 – Stimulation in the popliteal fossa
G – Ground
R – Reference

Photograph – 2

Recording of nerve conductions parameters of median never (motor) in a diabetic

BRAINSTEM AUDITORY EVOKED POTENTIALS[28].

Brainstem auditory evoked potentials are the potentials recorded from the ear and vertex in response to a brief auditory stimulation to assess the conduction through the auditory pathway upto midbrain. Brainstem auditory evoked potentials comprise 5 or more peaks within 10 ms of the stimulus.

The auditory nerve and brainstem auditory potentials are volume conduction to surface electrodes. At the vertex and earlobe, these form vertex positive and vertex negative waves which are known as brainstem auditory evoked potentials. The peak to peak amplitude of these waves recorded from the scalp are only about 1/00 the amplitude of ongoing spontaneous EEG activity. There are 5 or more distinct waveforms recorded within 10 ms of the auditory stimulus.

Origin of brainstem auditory evoked potentials

I VIII NERVE

II COCHLEAR NUCLEUS

III SUPERIOR OLIVORY NUCLEUS

IV LATERAL LEMNISCUS

V INFERIOR COLLICULI

INSTRUMENT SETTINGS FOR RECORDING BAEPs

ELECTRODES

Surface electrodes were used to record electrophysiological signals produced in the auditory pathway in response to auditory stimulus. The electrodes were standard cup type silver – silver chloride electrodes of 10mm diameter and 1.5 m in length.

MONTAGE SETTINGS

Active electrode – ipsilateral mastoid.

Reference electrode – vertex (Cz).

Ground electrode - contra lateral mastoid.

AMPLIFIER AND AVERAGER.

BAEPs are recorded using an amplification of 200000 - 500000. A 10 ms epoch after the stimulus is averaged for BAEP recording and about 2000 trials are averaged to get a good quality recording. Two repetitions are done and superimposed to get a good quality recording.

FILTER SETTINGS

Low frequency filter – 100 Hz, electrical activity with frequencies lower than 100 Hz like electroencephalogram activity or other low frequency electrical noise are filtered.

High frequency filter – 3000 Hz.

AUDITORY STIMULATION

Auditory stimulation is produced via headphones fitted to the person's ear. The BAEPs are produced by a brief click stimulus which is a square wave pulse of 0.1 ms duration.

Click rate – 11 Hz.

Click intensity – 90 Db.

Masking – white noise at 60 db intensity.

PROCEDURE

Using electrode paste, the recording electrode was placed at ipsilateral mastoid (the ear to which click stimulus is to be given) the reference electrode was placed at Cz midline in the vertex. The ground electrode was placed in the contra lateral mastoid. The electrodes were connected to the pre–amplifier. The subject is asked not to move his/her head during the test. **Refer Photograph 3**

Photograph - 3

RESULTS

40 type 2 diabetic patients and 40 healthy controls were included in this study. Nerve conduction tests of median sensory, median motor and tibial motor were performed. Latency, amplitude and nerve conduction velocity were measured.

Brainstem auditory evoked potential of both the ears was tested. Absolute and interpeak latencies were measured.

Diabetic patients were divided into two groups based on duration of disease.

Group 1 – 0-7 years diabetes duration (20 patients).

Group 2 – 7- 15 years diabetes duration (20 patients).

Results were analysed by student's independent t-test.

P –value was calculated to test the statistical significance.

P- value <0.05 was considered significant.

P- value <0.01 was considered highly significant.

P- value <0.001 was considered very highly significant.

1) COMPARISON OF NERVE CONDUCTION VALUES BETWEEN DIABETICS AND CONTROLS

1.1 Comparison of latency of median nerve-sensory, median nerve-motor and tibial nerve-motor between diabetics and controls.

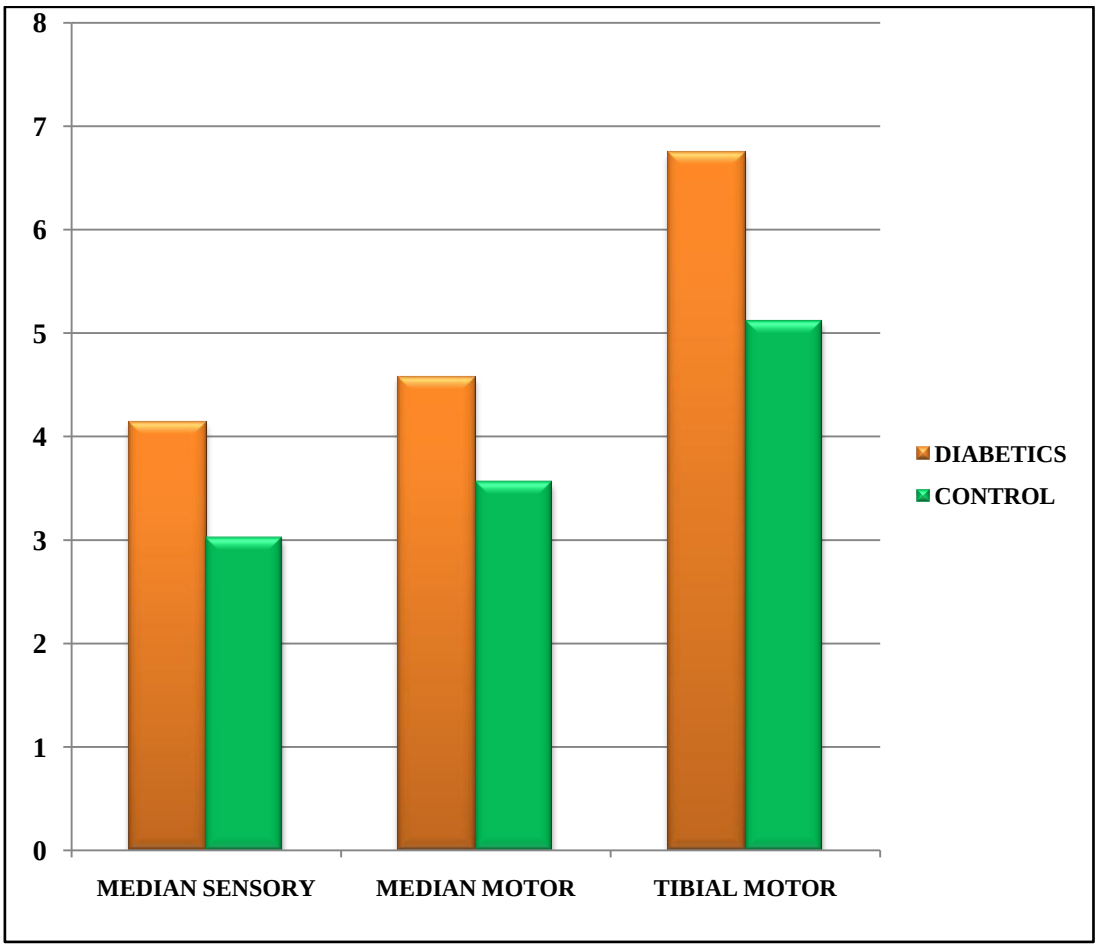
NERVE TESTED	GROUPS	NO OF SUBJECTS	MEAN ± SD (ms)	P-VALUE
Median nerve-sensory	Diabetic	40	4.14 ± 0.96	<0.001
	Control	40	3.02 ± 0.32	
Median nerve-motor	Diabetic	40	4.57 ± 1.29	<0.001
	Control	40	3.56 ± 0.28	
Tibial nerve-motor	Diabetic	40	6.74 ± 1.32	<0.001
	Control	40	5.11 ± 0.55	

P = < 0.001 is very highly significant

There was a very highly significant increase in the latency of median nerve (sensory and motor) and tibial nerve (motor) in the diabetic group compared to the controls.

Comparison of latency of median nerve-sensory, median nerve-motor and tibial nerve-motor between diabetics and controls. (ms)

Plate 1.1



1.2 Comparison of amplitude of median nerve-sensory, median nerve-motor and tibial nerve-motor between diabetics and controls.

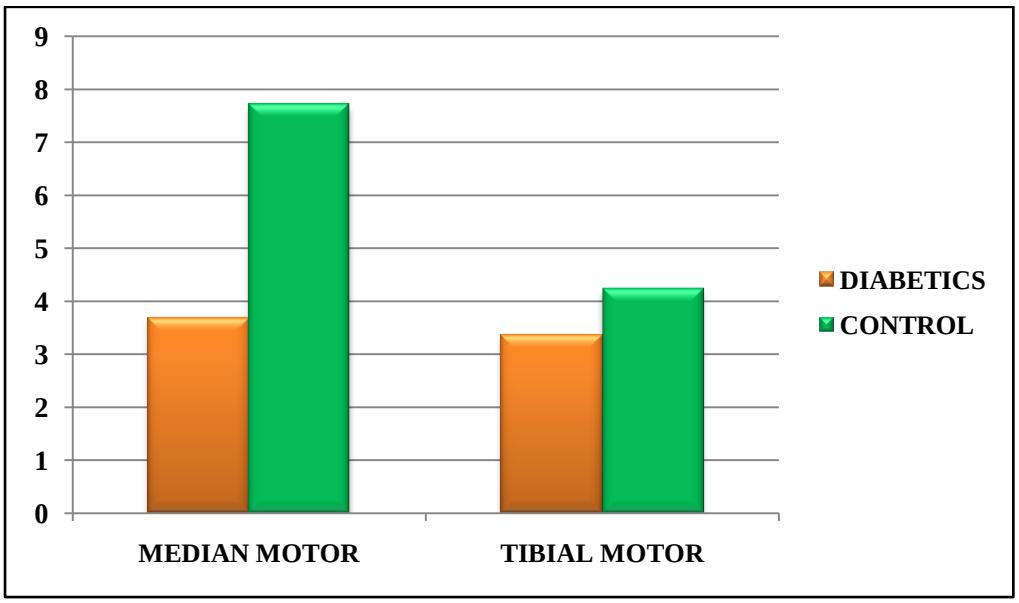
NERVE TESTED	GROUPS	NO OF SUBJECTS	MEAN ± SD	P-VALUE
Median nerve-sensory (µv)	Diabetic	40	22.03 ± 4.50	<0.001
	Control	40	33.96 ± 3.95	
Median nerve-motor (mv)	Diabetic	40	3.69 ± 1.09	<0.001
	Control	40	7.70 ± 1.22	
Tibial nerve motor (mv)	Diabetic	40	3.38 ± 0.61	<0.001
	Control	40	4.23 ± 0.37	

P = < 0.001 is very highly significant

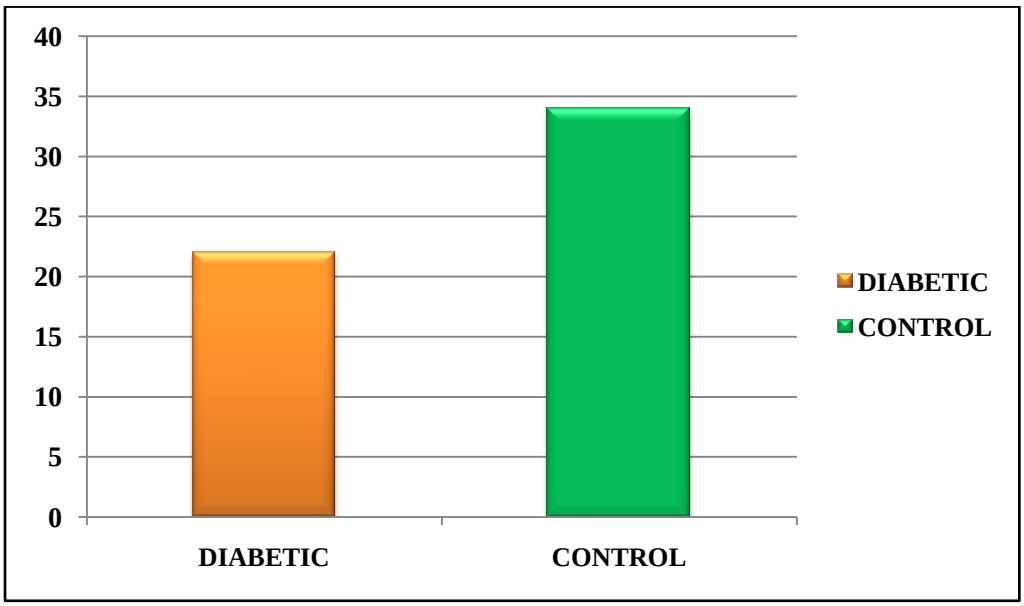
There was a very highly significant decrease in the amplitude of median nerve (sensory and motor) and tibial nerve (motor) in the diabetic group compared to the controls.

Comparison of amplitude of median nerve-motor and tibial nerve-motor between diabetics and controls. (mv)

Plate 1.2a :



Comparison of amplitude of median nerve-sensory between diabetics and controls. (µv) plate 1.2b :



1.3 Comparison of NCV of median nerve-sensory, median nerve-motor and tibial nerve-motor between diabetics and controls.

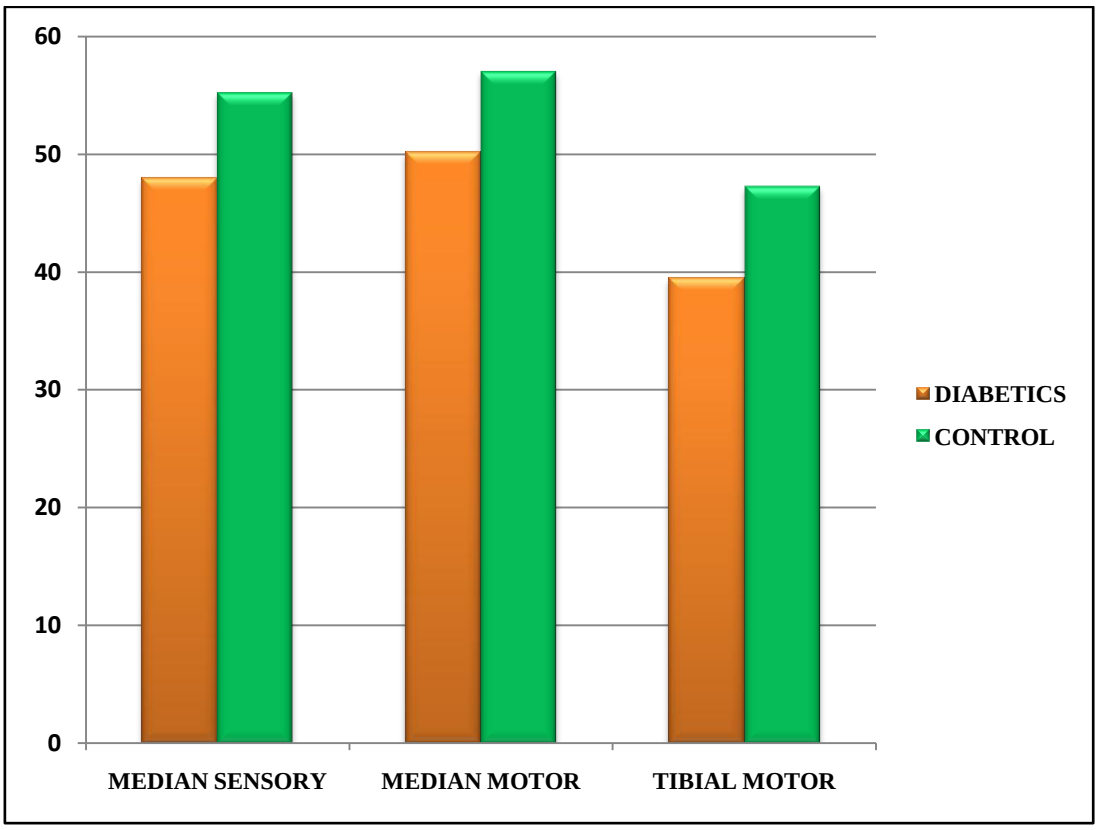
NERVE TESTED	GROUPS	NO OF SUBJECTS	MEAN ± SD (m/s)	P-VALUE
Median nerve-sensory	Diabetic	40	47.92 ± 3.73	<0.001
	Control	40	55.21 ± 3.01	
Median nerve-motor	Diabetic	40	50.11 ± 5.00	<0.001
	Control	40	57.01 ± 2.31	
Tibial nerve - motor	Diabetic	40	39.42 ± 3.91	<0.001
	Control	40	47.26 ± 1.10	

P = < 0.001 is very highly significant

There was a very highly significant decrease in the NCV of median nerve (sensory and motor) and tibial nerve (motor) in the diabetic group compared to the controls.

Comparison of NCV of median nerve-sensory, median nerve-motor and tibial nerve-motor between diabetics and controls. (m/s)

Plate 1.3



2) COMPARISON OF NERVE CONDUCTION VALUES WITHIN DIABETICS DIVIDED INTO GROUPS BASED ON DURATION.

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

2.1 Comparison of latency of median nerve-sensory, median nerve-motor and tibial nerve-motor between two groups of diabetics.

S.NO	GROUPS	NO OF SUBJECTS	MEAN ± SD (ms)	P-VALUE
Median nerve-sensory	Group 1	20	3.71 ± 0.81	<0.01
	Group 2	20	4.57± 0.93	
Median nerve-motor	Group 1	20	4.13 ± 1.21	<0.05
	Group 2	20	5.01 ± 1.24	
Tibial nerve - motor	Group 1	20	6.25 ± 1.29	<0.05
	Group 2	20	7.22 ± 1.18	

P = < 0.01 is highly significant

P = < 0.05 is significant

There was a highly significant increase in the latency of median nerve (sensory) in group 2 compared to group 1.

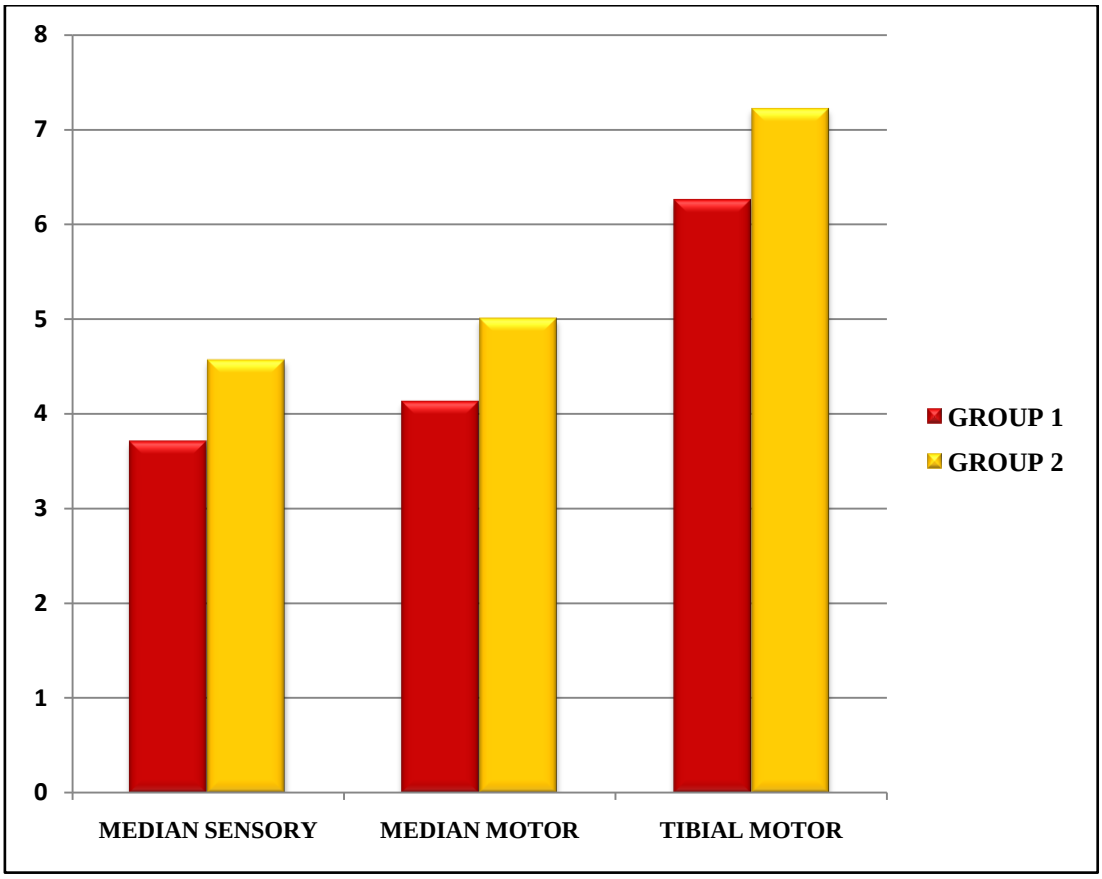
There was a significant increase in the latency of median nerve (motor) and tibial nerve (motor) in group 2 compared to group 1.

Comparison of latency of median nerve-sensory, median nerve-motor and tibial nerve-motor between two groups of diabetics. (ms)

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Plate 2.1



2.2 Comparison of amplitude of median nerve-sensory, median nerve-motor and tibial nerve-motor between two groups of diabetics

Group 1 – 0-7 years duration (20 patients).

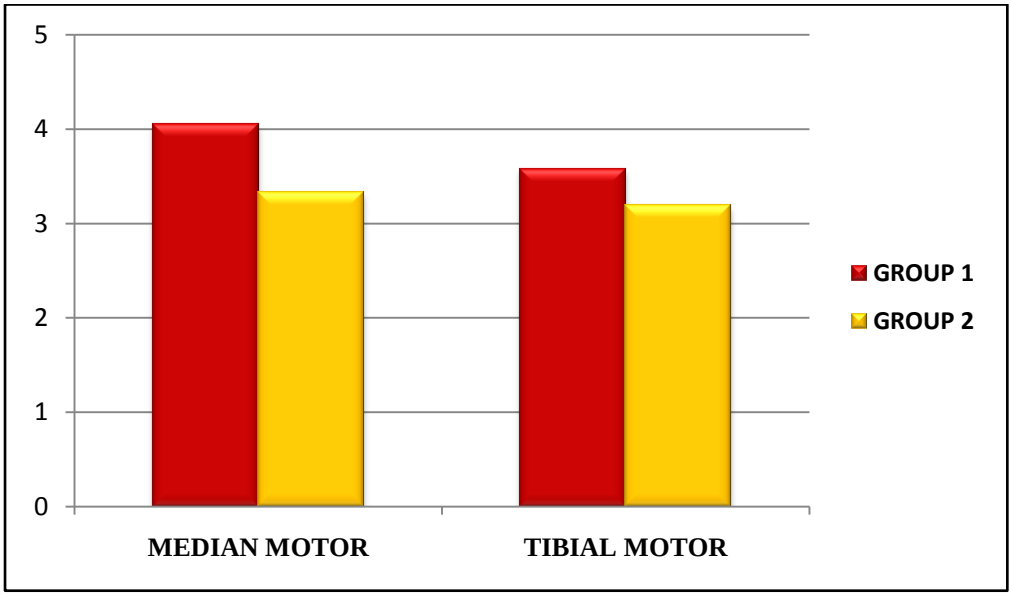
Group 2 –7-15 years duration (20 patients).

S.NO	GROUPS	NO OF SUBJECTS	MEAN ± SD	P-VALUE
Median nerve-sensory (μv)	Group 1	20	23.69 ± 4.37	<0.05
	Group 2	20	20.36 ± 4.09	
Median nerve-motor (mv)	Group 1	20	4.05 ± 0.92	<0.05
	Group 2	20	3.33 ± 1.15	
Tibial nerve motor (mv)	Group 1	20	3.58 ± 0.66	<0.05
	Group 2	20	3.19 ± 0.51	

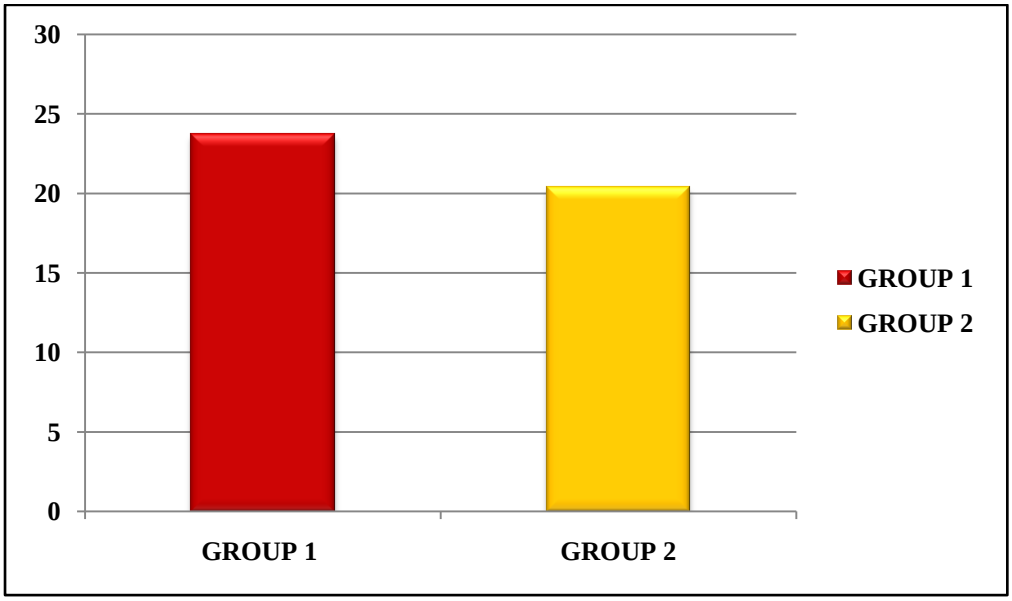
P = < 0.05 is significant

There was a significant decrease in the amplitude of median nerve (sensory and motor) and tibial nerve (motor) in group 2 compared to group 1.

Comparison of amplitude of median nerve-motor and tibial nerve-motor between two groups of diabetics. plate 2.2a



Comparison of amplitude of median nerve sensory between two groups of diabetics plate 2.2b



2.3 Comparison of NCV of of median nerve-sensory, median nerve-motor and tibial nerve-motor between two groups of diabetics.

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

S.NO	GROUPS	NO OF SUBJECTS	MEAN ± SD (m/s)	P-VALUE
Median nerve-sensory	Group 1	20	49.62 ± 3.35	<0.01
	Group 2	20	46.23 ± 3.36	
Median nerve-motor	Group 1	20	51.69 ± 4.64	<0.05
	Group 2	20	48.53 ± 4.95	
Tibial nerve - motor	Group 1	20	41.11 ± 3.86	<0.01
	Group 2	20	37.48 ± 3.25	

P = < 0.01 is highly significant

P = < 0.05 is significant

There was a highly significant decrease in the NCV of median nerve (sensory) and tibial nerve (motor) in group 2 compared to group 1.

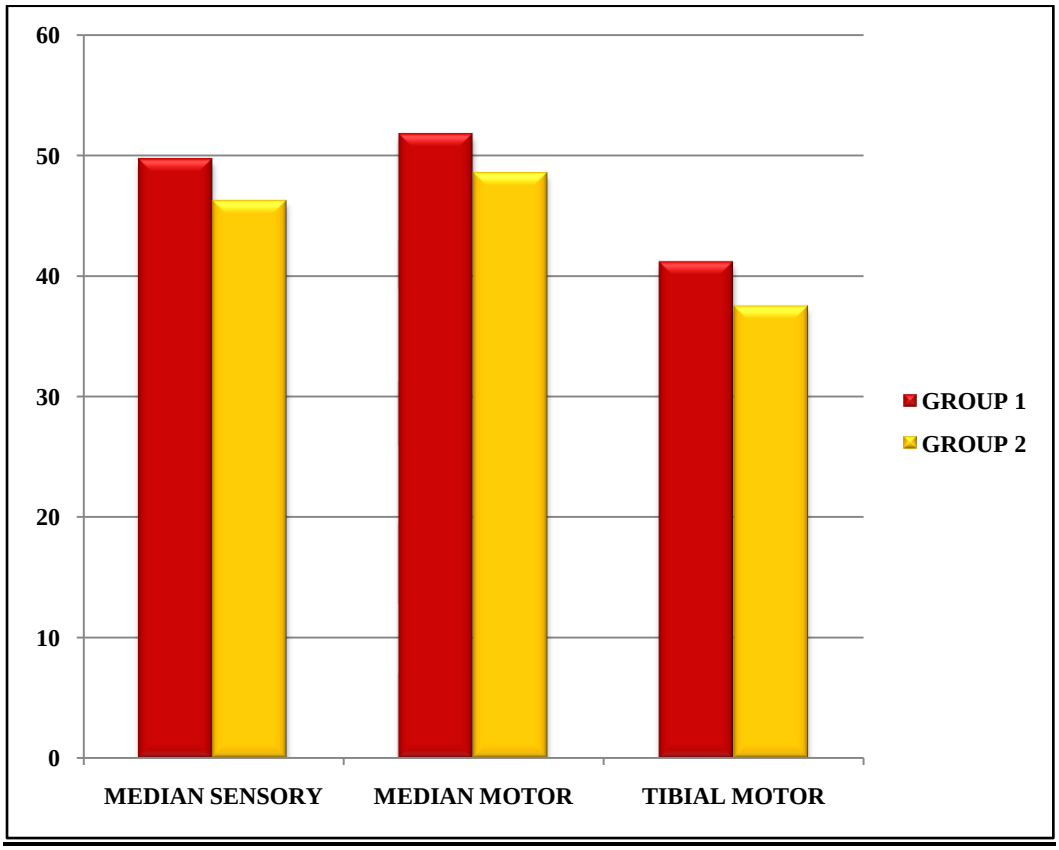
There was a significant decrease in the NCV of median nerve (motor) in group 2 compared to group 1.

Comparison of NCV of of median nerve-sensory, median nerve-motor and tibial nerve-motor between two groups of diabetics. (m/s)

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Plate 2.3



BAEP RESULTS

3.1 Comparison of absolute latencies of BAEP between diabetics and controls – RIGHT EAR:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD	P -value
WAVE -I	Diabetic	40	1.49 ± 0.05	0.539
	Control	40	1.48 ± 0.05	
WAVE -II	Diabetic	40	2.73 ± 0.10	0.088
	Control	40	2.77 ± 0.09	
WAVE -III	Diabetic	40	3.79 ± 0.14	<0.001
	Control	40	3.56 ± 0.05	
WAVE -IV	Diabetic	40	4.95 ± 0.10	0.404
	Control	40	4.93 ± 0.06	
WAVE -V	Diabetic	40	6.24 ± 0.42	<0.001
	Control	40	5.69 ± 0.06	

P = < 0.001 is very highly significant

P = >0.05 not significant

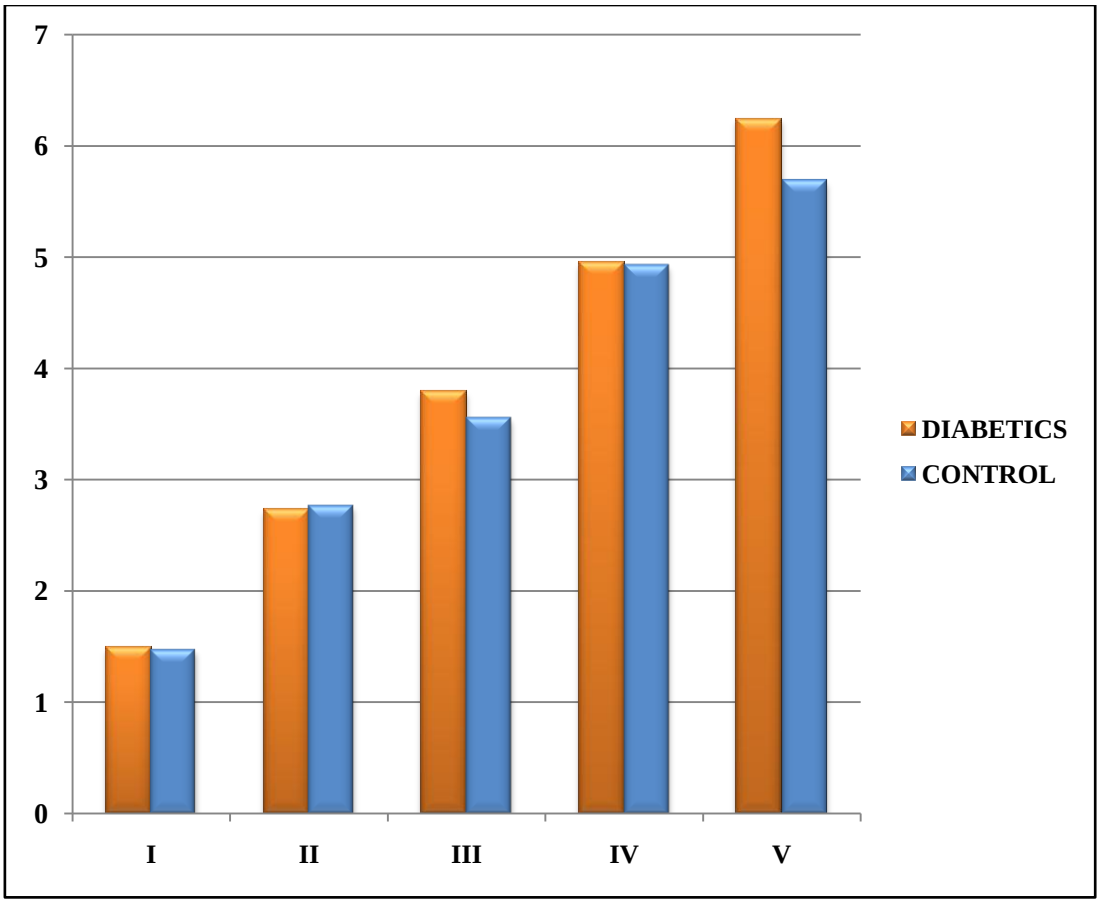
There was a very highly significant increase in the absolute latency of wave III and V in diabetics compared to the controls.

There was no significant difference in the absolute latency of wave I, II and IV in diabetics compared to the controls.

Comparison of absolute latencies of BAEP between diabetics and controls.

RIGHT EAR:

Plate 3.1



3.2 Comparison of absolute latencies of BAEP between diabetics and controls –LEFT EAR:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD (ms)	P -value
WAVE -I	Diabetic	40	1.50 ± 0.06	0.315
	Control	40	1.48 ± 0.04	
WAVE -II	Diabetic	40	2.76 ± 0.11	0.935
	Control	40	2.76 ± 0.15	
WAVE -III	Diabetic	40	3.79 ± 0.21	<0.001
	Control	40	3.58 ± 0.06	
WAVE -IV	Diabetic	40	4.97 ± 0.12	0.125
	Control	40	4.94 ± 0.06	
WAVE -V	Diabetic	40	6.25 ± 0.44	<0.001
	Control	40	5.70 ± 0.07	

P = < 0.001 is very highly significant

P = >0.05 not significant

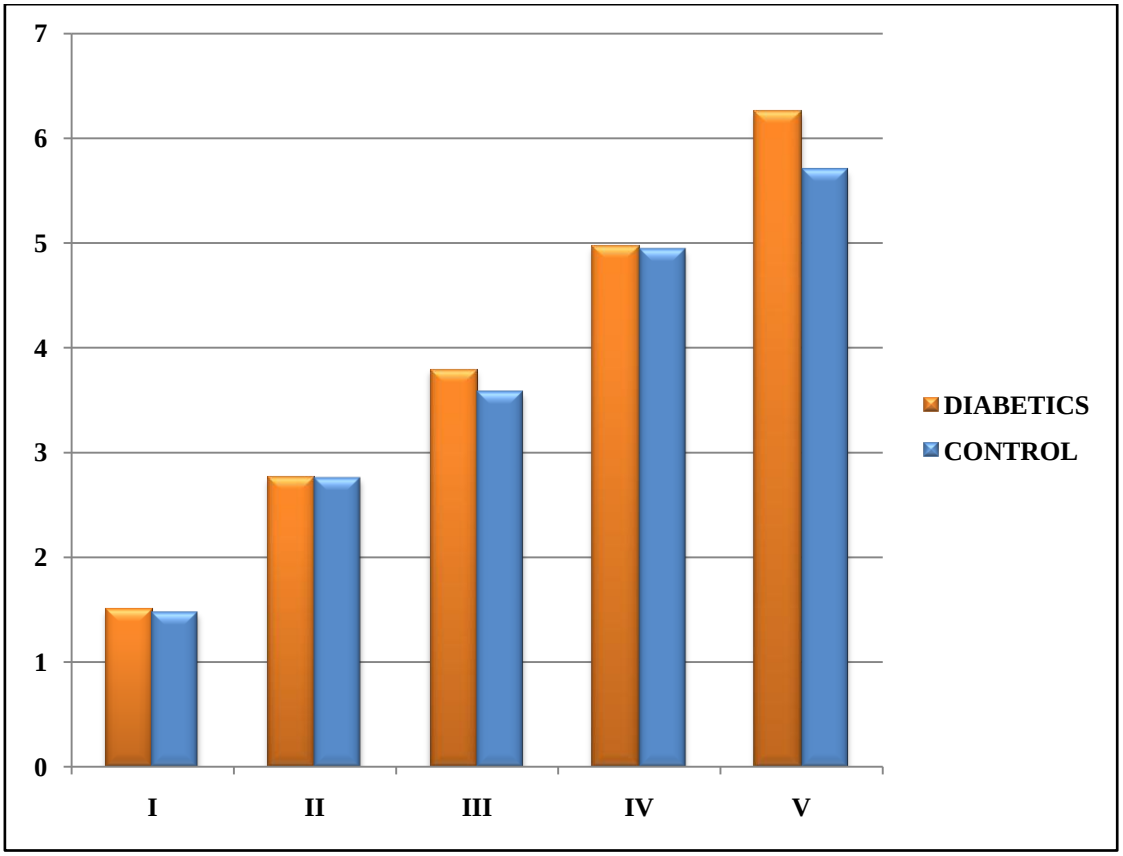
There was a very highly significant increase in the absolute latency of wave III and V in diabetics compared to the controls.

There was no significant difference in the absolute latency of wave I, II and IV in diabetics compared to the controls.

Comparison of absolute latencies of BAEP between diabetics and controls.

LEFT EAR:

Plate 3.2



3.3 Comparison of interpeak latencies of BAEP between diabetics and controls

RIGHT EAR:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD(ms)	P - value
I-III INTERPEAK LATENCY	Group 1	40	2.30 ± 0.17	<0.001
	Group 2	40	2.08 ± 0.07	
I-III INTERPEAK LATENCY	Group 1	40	4.75 ± 46	<0.001
	Group 2	40	4.20± 0.08	
I-III INTERPEAK LATENCY	Group 1	40	2.45 ± 0.32	<0.001
	Group 2	40	2.12 ± 0.09	

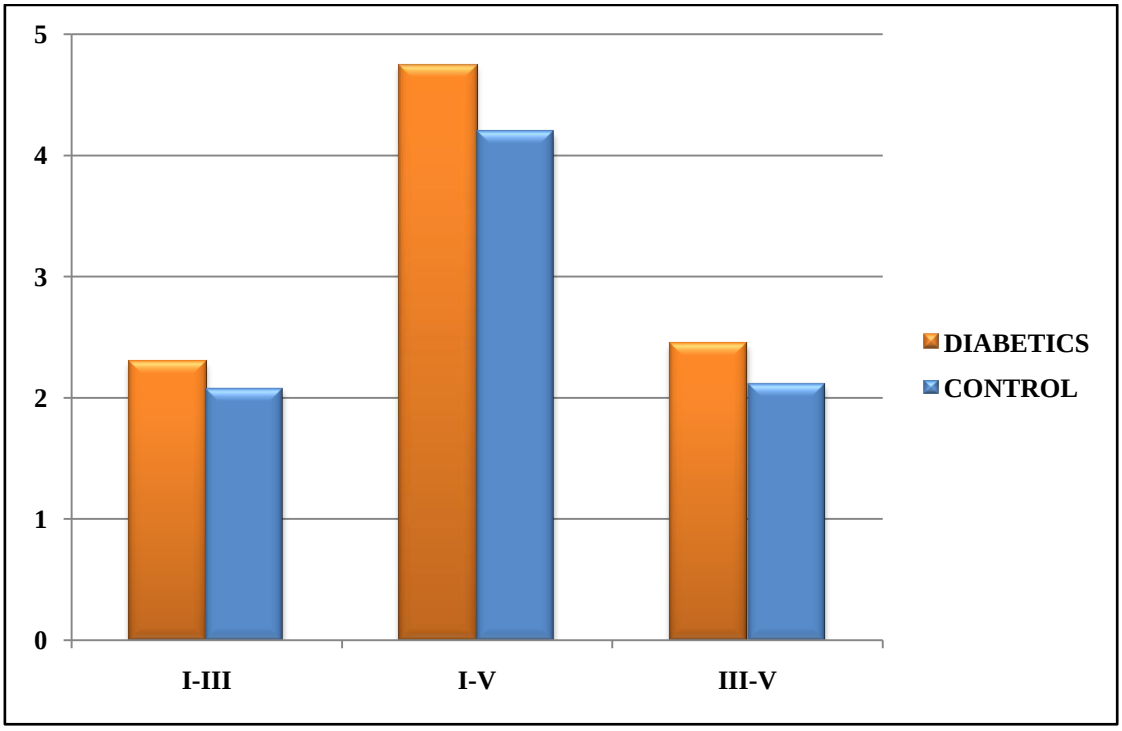
P = < 0.001 is very highly significant

There was a very highly significant increase in the I-III, I-V, and III-V interpeak latency of diabetics compared to the controls.

Comparison of interpeak latencies of BAEP between diabetics and controls

RIGHT EAR:

Plate 3.3



3.4 Comparison of interpeak latencies of BAEP between diabetics and controls

LEFT EAR:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ± SD (ms)	P-value
I-III INTERPEAK LATENCY	Diabetic	40	2.29 ± 0.25	<0.001
	Control	40	2.09 ± 0.08	
I-V INTERPEAK LATENCY	Diabetic	40	4.75 ± 0.48	<0.001
	Control	40	4.21 ± 0.09	
III-V INTERPEAK LATENCY	Diabetic	40	2.46 ± 0.35	<0.001
	Control	40	2.12 ± 0.09	

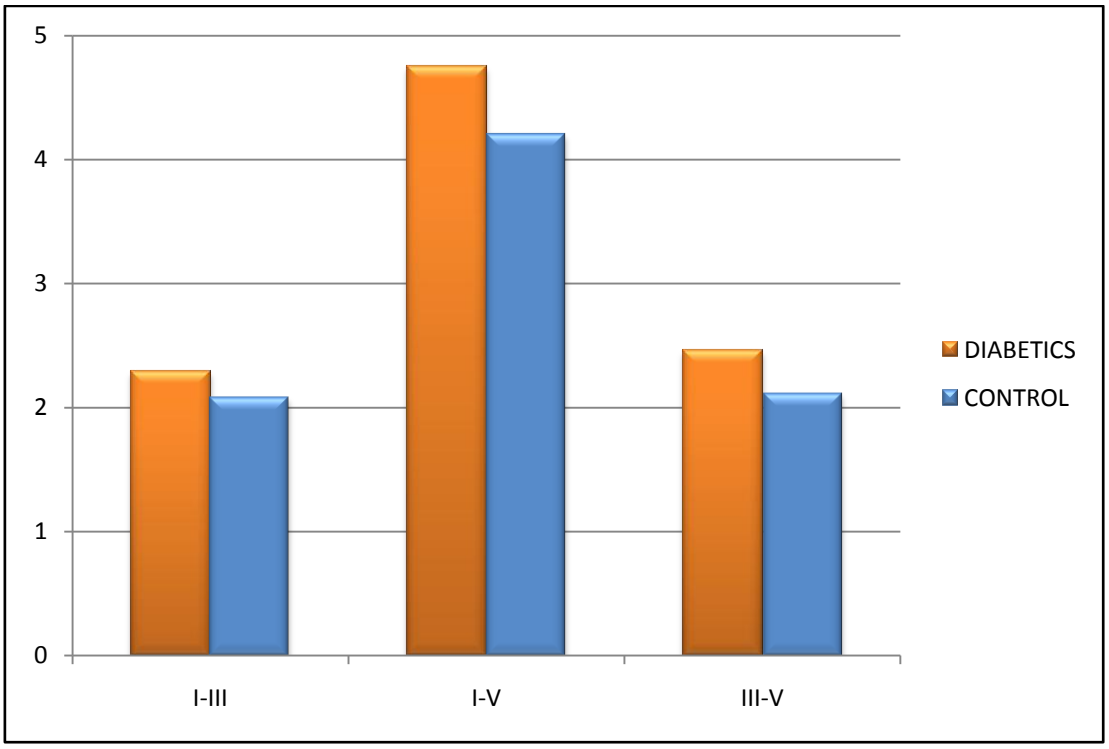
P = < 0.001 is very highly significant

There was a very highly significant increase in the I-III, I-V, and III-V interpeak latency of diabetics compared to the controls.

3.4 Comparison of interpeak latencies of BAEP between diabetics and controls

LEFT EAR:

Plate 3.4



4.1 Comparison of absolute latencies of BAEP within diabetics divided into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Right ear:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ±SD(ms)	P -value
WAVE -I	Group 1	20	1.50 ± 0.05	0.08
	Group 2	20	1.47 ± 0.05	
WAVE -II	Group 1	20	2.71 ± 0.10	0.246
	Group 2	20	2.75 ± 0.11	
WAVE -III	Group 1	20	3.77 ± 0.16	0.447
	Group 2	20	3.81 ± 0.12	
WAVE -IV	Group 1	20	4.94 ± 0.09	0.920
	Group 2	20	4.95 ± 0.12	
WAVE -V	Group 1	20	6.08 ± 0.31	<0.05
	Group 2	20	6.41 ± 0.46	

P = < 0.05 is significant

P = > 0.05 is not significant

There was a significant increase in the absolute latency of wave V in group 2 compared to group 1.

There was no significant difference in the absolute latency of wave I, II, III, and IV in group 2 compared to group 1.

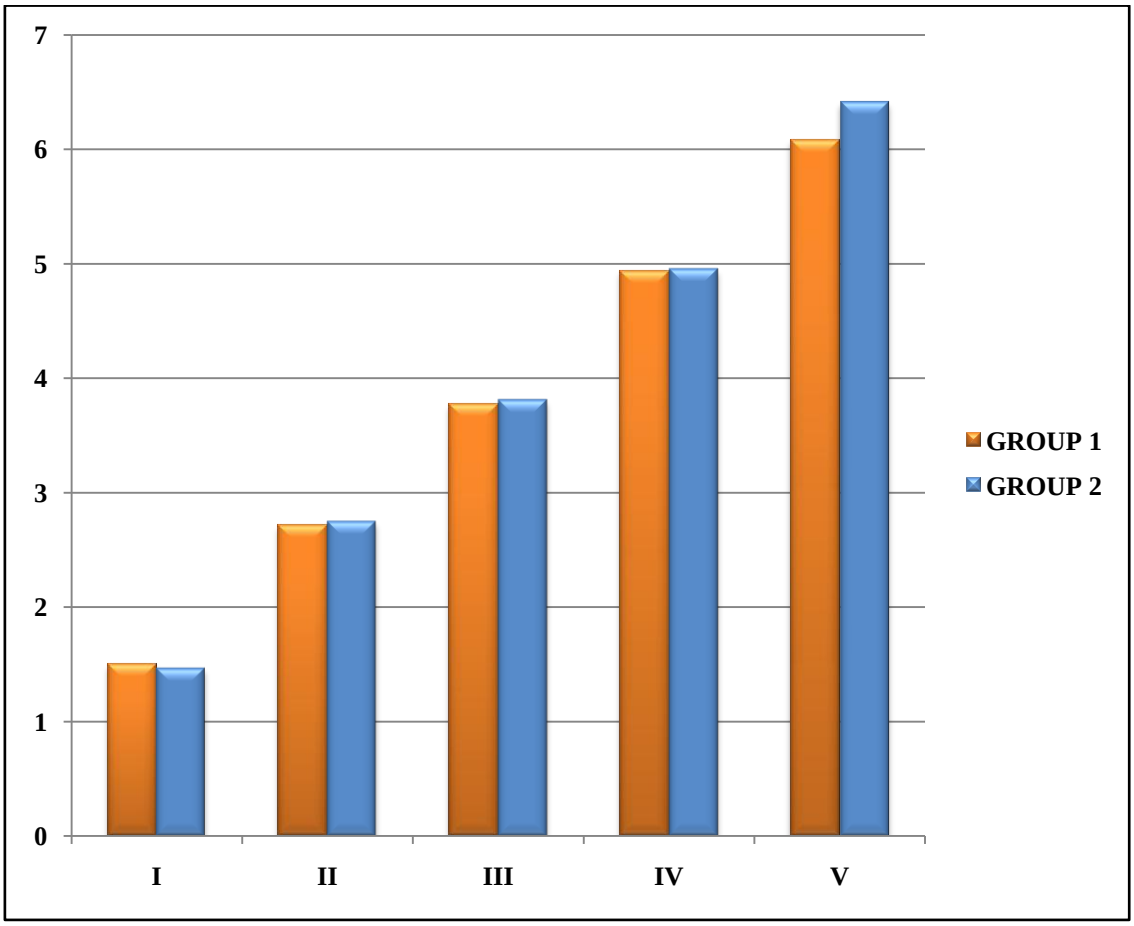
Comparison of absolute latencies of BAEP within diabetics divided into groups based on duration.

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Right ear:

Plate 4.1



4.2 Comparison of absolute latencies of BAEP within diabetics divided into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Left Ear:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ±SD(ms)	P -value
WAVE -I	Group 1	20	1.51 ± 0.06	0.084
	Group 2	20	1.48± 0.05	
WAVE -II	Group 1	20	2.75 ± 0.11	0.723
	Group 2	20	2.77± 0.12	
WAVE -III	Group 1	20	3.79± 0.16	0.971
	Group 2	20	3.79± 0.26	
WAVE -IV	Group 1	20	4.97 ± 0.11	0.863
	Group 2	20	4.97 ± 0.13	
WAVE -V	Group 1	20	6.05± 0.34	<0.01
	Group 2	20	6.46± 044	

P = < 0.01 is highly significant

p = > 0.05 is not significant

There was a highly significant increase in the absolute latency of wave V in group 2 compared to group 1.

There was no significant difference in the absolute latency of wave I, II, III, and IV in group 2 compared to group 1.

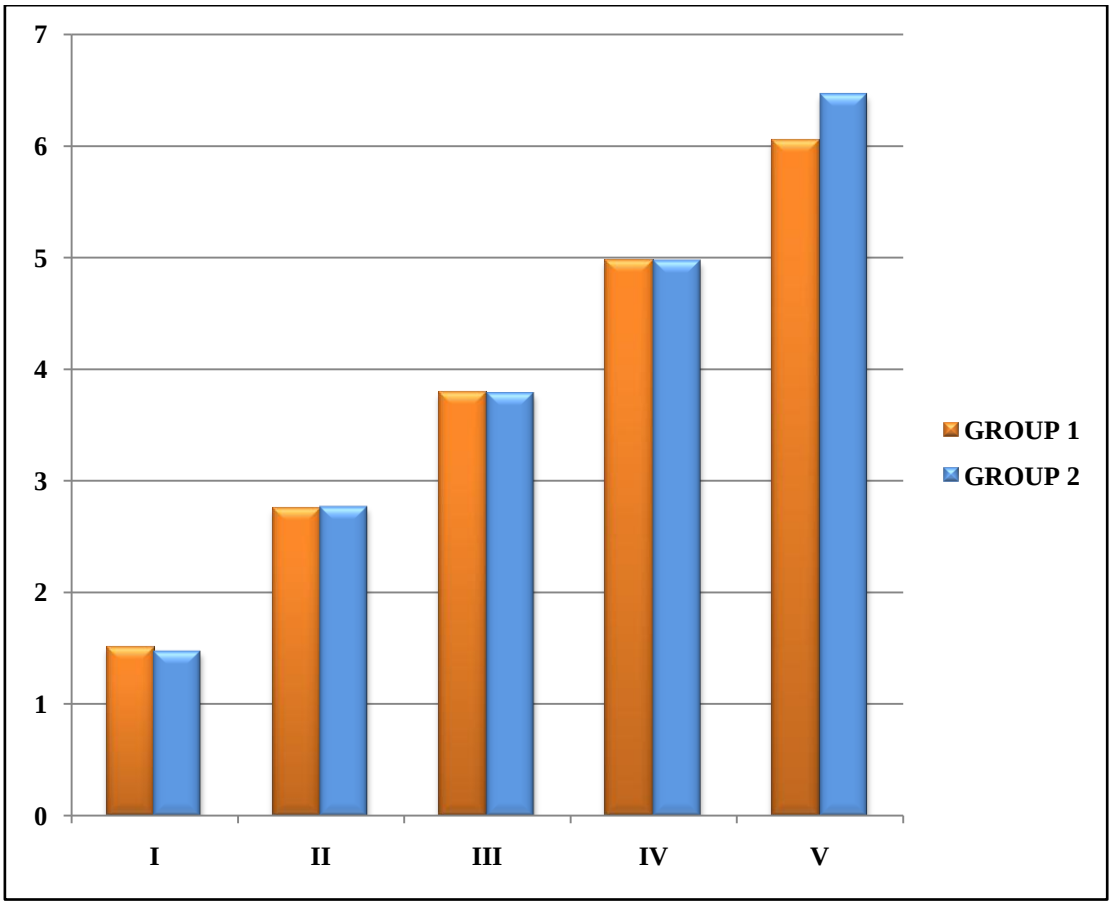
Comparison of absolute latencies of BAEP within diabetics divided into groups based on duration.

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Left Ear:

Plate 4.2



4.3 Comparison of interpeak latencies of BAEP within diabetics divided into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Right Ear:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ±SD(ms)	P -value
I-III INTERPEAK LATENCY	Group 1	20	2.27 ± 0.19	0.253
	Group 2	20	2.33 ± 0.15	
I-V INTERPEAK LATENCY	Group 1	20	4.57 ± 0.34	<0.05
	Group 2	20	4.93 ± 0.50	
III-V INTERPEAK LATENCY	Group 1	20	2.30 ± 0.18	<0.01
	Group 2	20	2.60 ± 0.36	

P = < 0.01 is highly significant.

P = < 0.05 is significant.

P = > 0.05 is not significant.

There was a highly significant increase in III-V interpeak latency in group 2 compared to group 1.

There was a significant increase in I-V interpeak latency in group 2 compared to group 1.

There was no significant diference in I-III interpeak latency in group 2 compared to group 1.

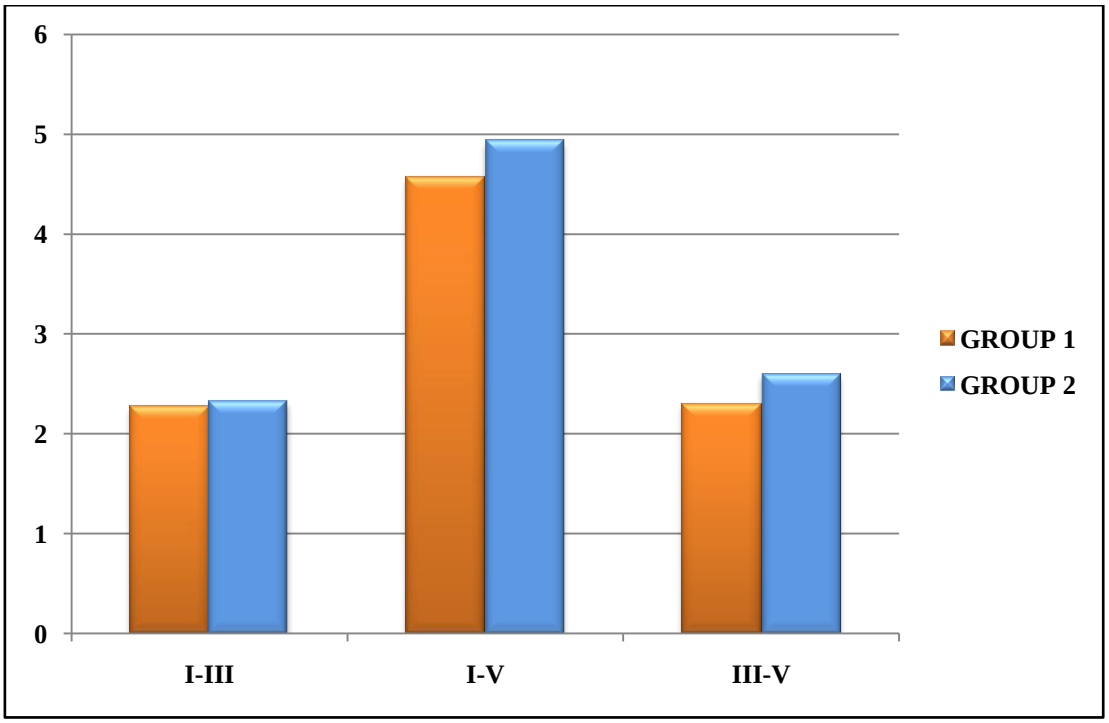
Comparison of interpeak latencies of BAEP within diabetics divide into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Right Ear:

Plate 4.3



4.4 Comparison of interpeak latencies of BAEP within diabetics divided into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Left Ear:

BAEP LATENCY (ms)	GROUP	NO OF SUBJECTS	MEAN ±SD(ms)	P -value
I-III INTERPEAK LATENCY	Group 1	20	2.27 ± 0.21	0.701
	Group 2	20	2.31 ± 0.28	
I-V INTERPEAK LATENCY	Group 1	20	4.53 ± 0.39	<0.01
	Group 2	20	4.93 ± 0.47	
III-V INTERPEAK LATENCY	Group 1	20	2.25 ± 0.18	<0.001
	Group 2	20	2.67 ± 0.36	

P=<0.001 very highly significant.

P = < 0.01 is highly significant.

P = > 0.05 is not significant.

There was a very highly significant increase in III-V interpeak latency in group 2 compared to group 1.

There was a highly significant increase in I-V interpeak latency in group 2 compared to group 1.

There was no significant difference in I-III interpeak latency in group 2 compared to group1.

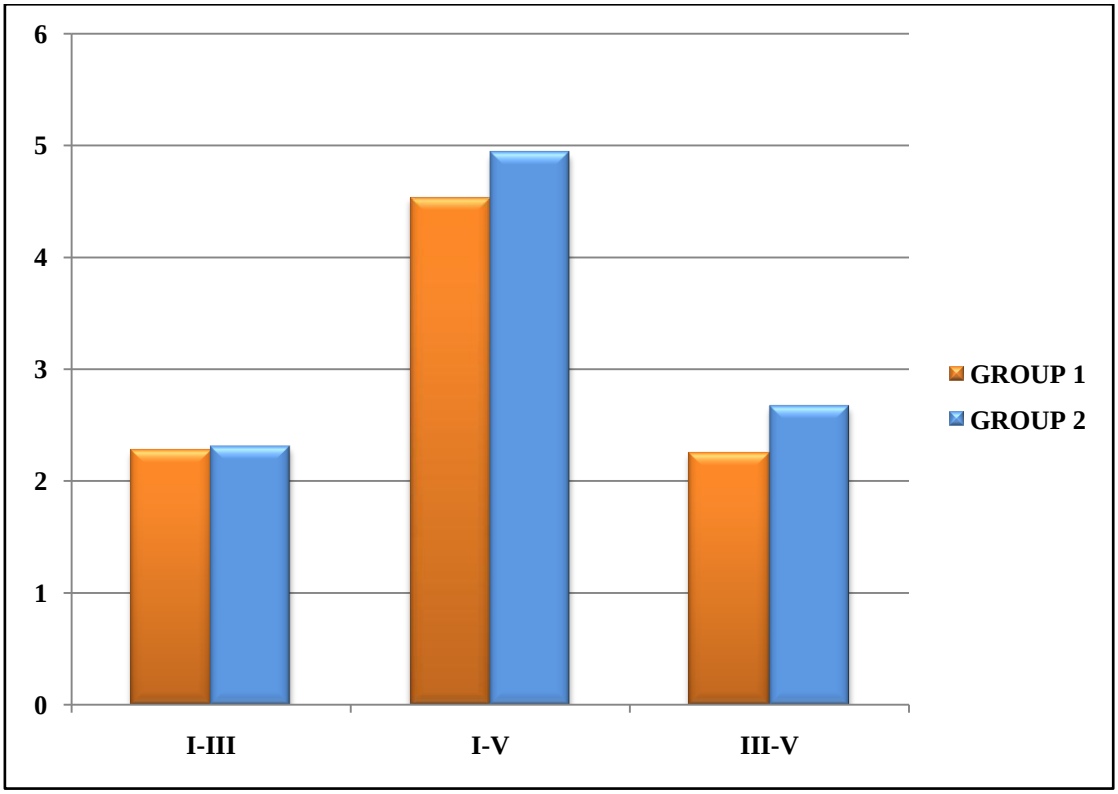
Comparison of interpeak latencies of BAEP within diabetics divide into groups based on duration

Group 1 – 0-7 years duration (20 patients).

Group 2 –7-15 years duration (20 patients).

Left Ear:

Plate 4.4



Number of diabetics with nerve conduction abnormality

Nerve conduction parameters affected

Type 2 Diabetics - 40 patients.

Controls - 40 healthy individuals.

Nerve	Prolonged latency		Reduced amplitude		Decreased NCV	
	Diabetics	**Control**	**Diabetics**	**Control**	**Diabetics**	**Control**
Median nerve - sensory	22	0	18	0	24	0
Median nerve - motor	20	0	17	0	23	0
Tibial nerve - motor	24	0	20	0	26	0

Nerve conduction parameters were most affected in the tibial nerve (motor).

There were no nerve conduction abnormalities in the controls.

Nerve Conduction Results within Diabetics Groups

Group 1 – 0-7 years diabetes duration (20 patients).

Group 2 – 7-15 years diabetes duration (20 patients).

Nerve	Prolonged latency		Reduced amplitude		Decreased NCV	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Median nerve - sensory	8	14	7	11	9	15
Median nerve - motor	7	13	6	11	9	14
Tibial nerve - motor	9	15	8	12	10	16

Number of diabetics with abnormal (increase) BAEP latency

S.NO	GROUP	NO OF SUBJECTS	BAEP LATENCY ABNORMALITY	
			PRESENT	ABSENT
1	DIABETICS	40	22	18
2	GROUP 1	20	8	12
3	GROUP 2	20	14	6

DISCUSSION

Nerve conduction studies and BAEP are simple, sensitive and objective technique for evaluating impulse conduction along the peripheral and central nervous systems. The present study deals with the abnormalities in nerve conduction study and BAEP in non insulin dependent diabetes mellitus patients.

In our study nerve conduction parameters of sensory and motor component of median nerve and motor component of tibial nerve were studied unilaterally (right side). In several clinical trials, nerve conduction studies were often used, and were shown to be symmetrical in patients with diabetic sensory and sensorimotor polyneuropathy, thus justifying unilateral evaluation [66.]

NERVE CONDUCTION ABNORMALITIES IN DIABETICS

Diabetic neuropathy (DN) is a common complication of DM and it is encountered in more than one third of diabetic patients[67]. Pirart J[31] had found a fivefold increase in the incidence of DN after 25 years of follow up. Discordance between nerve conduction studies and symptoms and signs of DN had been reported before [68, 69.] In our study we found out abnormalities in all the parameters of nerve conduction study in diabetics when compared with controls.

In our study a statistically significant difference was noted between the study group and control group in latencies of all the nerves tested viz., sensory and motor division of median nerve and tibial nerve. We also

observed a significant decrease in the amplitude and nerve conduction velocity of all the nerves tested in diabetics when compared with controls.

Both latency and nerve conduction velocity depend on an intact, myelinated nerve as myelin and the saltatory conduction are essential for fast action potential propagation in normal subjects. In contrast, the amplitude of the waveform depends primarily on number of axons functioning within the nerve. Slowing of conduction velocity or prolongation of latency usually implies demyelinating injury, while loss of amplitude usually correlates with axonal loss or dysfunction [7].

In our study it was found out that latency and nerve conduction velocity were more affected than amplitude which is explained by the fact that DN is predominantly demyelinating [70,71].

Among the nerves tested tibial nerve was most affected with 26 of the 40 diabetics showing abnormal conduction parameters. The involvement of sensory and motor division of median nerve was almost uniform, 24 diabetics with median sensory neuropathy and 23 with median motor neuropathy. The tibial nerve involvement can be explained by the fact that distal polyneuropathy is the most common neuropathy in DM and lower limb nerves are more involved than the upper limbs[72]. The uniform involvement of sensory and motor division of median nerve can be evidenced by the studies conducted by Fagerberg et al[50], Gregersen[49] and Bril[73] who reported that motor defects are common in diabetics with neuropathy and increase in frequency with the duration of the disease. Jun Kimura et al [74] reported distal slowing of motor nerve conduction velocity in diabetic polyneuropathy.

EFFECT OF DURATION ON NERVE CONDUCTION PARAMETERS

Though people with diabetes can develop neurological problems at any time, the risk of developing neuropathy increases with the duration of diabetes [75]. In our study we found that duration of the disease had an influence on the nerve conduction parameters and found that latency delay and reduction in amplitude and nerve conduction velocity of the tested nerves was of greater degree in diabetics with longer duration (7-15 years) and were statistically significant when compared with diabetics in the 0-7 years duration group. It was also found that mean amplitude of the nerves tested were normal in 0-7 year diabetic group whereas latency and NCV showed abnormalities even in this group. This could be explained by previous studies which stated that in diabetic neuropathy of shorter duration, segmental demyelination may be the only abnormal finding [76], whereas combined axonal and myelin changes suggesting wallerian degeneration are found in chronic or severe cases [77].

In a study done by Abdulsalam A et al[78], the affected nerve conduction parameters in early diabetics were latencies and NCVs, whereas the amplitudes of sensory and motor responses were not significantly different from the control. This suggests that the early diabetic effects on the peripheral nerves were mainly demyelinating.

The reduction in amplitude of nerve potential with duration may be explained by axonal injury. This could be the result either of a conduction block in fibres demyelinated for a long distance or of the degeneration of a number of axons[79].

As per the previous studies, the severity of neuropathy increases with age and duration of diabetes [80]. Aaron I Vinik found that duration of diabetes correlated with all three nerve conduction parameters [46].

BAEP LATENCIES IN DIABETES

In our study we found out that about 22 diabetics showed BAEP latency abnormalities. In our study, the absolute latencies of wave III and wave V and the interpeak latencies I-III, I-V and III-V were increased in DM group which showed a significant statistical difference when compared with the control group. The absolute latencies of wave I and wave II were normal in the study group suggesting that eighth nerve transmission time was normal in the diabetics. The increase in wave III latency and interpeak latency I – III with normal wave I and II latency indicates that there may be a dysfunction in the lower brainstem. Involvement of brainstem is also evidenced by an increase in absolute latency of wave V, I-V and III-V interpeak latencies .The BAEP findings of this study indicates that there may be involvement of brain stem in diabetic patients as evidenced by previous studies.[57, 81, 82]

In our study we also found out the impact of diabetes duration on BAEP latencies .The latency prolongation is more pronounced in 7-15 (group I) years disease duration group compared to 0-7 years group (group II). The latency of wave V and interpeak latencies III–V and I-V showed a significant statistical difference among the above two groups.

This finding can be supported by the studies conducted by M W Donald et al[60] and Ashok Verma et al [83]. In the study conducted by M W Donald et al[60] the mean duration of illness was 16 years and he observed a prolongation of III, V latencies and I-III , I-V interpeak latencies. In the study conducted by Ashok Verma et al [83] the mean duration of illness was 6 years and there was no increase in BAEP latencies among the diabetics. Olsson et al[61] and Reske-Nielsen et al[11] on the basis of detailed pathoanatomic studies, concluded that brain involvement was common in long standing diabetes.

ABNORMALITIES IN NERVE CONDUCTION AND BRAINSTEM AUDITORY EVOKED POTENTIALS IN DIABETICS.

In the present study it was found that both BAEP latency and nerve conduction parameters showed significant abnormality in diabetic individuals. BAEP abnormality was observed only in those subjects with abnormal nerve conduction parameters. A correlation between the BAEP findings and nerve conduction studies has been suggested, including velocity of median sensory and peroneal motor nerve in previous studies[84,85]. Chi-Ren Huang et al [59] reported that patients with DM had a delay in IPL I-III and IPL I-V in BAEP studies, especially in the neuropathy subgroup.

The peripheral neuropathy associated with diabetes mellitus is responsible for a myriad of syndromes. Whether a specific involvement of central nervous system also occurs, has been questioned. Major text books on diabetes either disregard cerebral involvement or minimise its

existence[86, 87]. However, a suggestion has been made recently that subclinical involvement occurs in diabetic patients[13, 15]. This study proves that there is involvement of central nervous system in diabetes as shown by increase in III, V absolute latencies and I-III ,I-V and III-V interpeak latencies which was also seen primarily in subjects with abnormal nerve conduction parameters thus suggesting that both central and peripheral nervous are involved in diabetes mellitus.

SUMMARY

40 type 2 diabetic individuals of both sex and 40 healthy controls were subjected to nerve conduction tests and brainstem auditory evoked potentials.

There was a significant increase in the latencies of nerve conduction parameter in non insulin dependent diabetic individuals.

There was a significant decrease in the amplitude and nerve conduction velocity of the peripheral nerves tested in diabetics.

Brainstem auditory evoked potential also showed a significant increase in the absolute latencies of wave III and V and interpeak latencies of I-III, I-V and III-V.

The latency delay and decrease in amplitude and nerve conduction velocity was significantly more pronounced in subjects with long duration of diabetes (7-15 years) when compared with short duration (0-7 years).

The duration of diabetes had a profound effect on Brainstem auditory evoked potential which showed a statistically significant increase in the latency of wave V and I-V and III-V interpeak latencies.

CONCLUSION

From this study it can be concluded that both the central and peripheral nervous systems are involved in diabetes mellitus as evidenced by an abnormal BAEP latencies and nerve conduction parameters.

There was a significant worsening of the condition as the duration of the diabetes increases in both the central and peripheral nervous systems. This shows that there may be progressive demyelination occurring along with axonal loss or dysfunction (decrease in amplitude) in DM.

This study suggests that periodic evaluation of diabetic individuals to such tests will help in monitoring the progress of neuropathy.

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ANNEXURE - I

8

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-600 003

Telephone 25363970
Fax 044 2535115
Dated : 12.05.2010

L.Dis.No.14597/ME5/Ethics Dean/MMC/2010

Title of the work : "Evaluation of Nerve Conduction Velocity and Brainstem Auditory Evoked Potential in type 2 Diabetes Mellitus Patients".

Principal Investigator : Dr. K. Kannan
Designation : PG in MD Physiology
Department :
MMC & GGH, Ch-3.

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 12th May 2010 at 2.p.m in Pharmacology Seminar Hall, Madras Medical College, Chennai -3

The members of the Committee, the Secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should get detailed informed consent from the patients/participants and maintain confidentiality.
2. You should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
3. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
4. You should not deviate form the area of the work for which you applied for ethical clearance.
5. You should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
6. You should abide to the rules and regulation of the institution(s).
7. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
8. You should submit the summary of the work to the ethical committee on completion of the work.
9. You should not claim funds from the Institution while doing the work or on completion.
10. You should understand that the members of IEC have the right to monitor the work with prior intimation.

SECRETARY
IEC, MMC,CHENNAI

CHAIRMAN
IEC,MMC, CHENNAI

DEAN
MADRAS MEDICAL COLLEGE,
CHENNAI -3

ANNEXURE – II

PROFORMA FOR CONDUCTING THE STUDY ON EVALUATION OF NERVE CONDUCTION ABNORMALITIES AND BRAINSTEM AUDITORY EVOKED POTENTIAL IN TYPE 2 DIABETES.

1. Name :
2. Age :
3. Sex :
4. Address :
5. Occupation :
6. Duration of diabetes :
7. Mode of treatment : Insulin

   Oral hypoglycemic drugs (or) both

8. Any other associated illness
   - (a) History of ischemic heart disease/stroke
   - (b) History of hypertension
   - (c) History of smoking
   - (d) History of alcoholism
   - (e) History of any ototoxic drug intake
   - (f) History of head injury
   - (g) History of any ear surgery
   - (h) History of numbness/pain in the Extremities
   - (i) History of drug intake cuasing neuropahy
   - (j) History of any endocrinopathy causing neuropathy

(k) Any vitamin deficiency

9. General examination (including detailed central nervous system and audiological examination)

10. Investigations

1. FBS mg/dl :

2. PPBS mg/dl :

11. Date of conduct of experiment :

EXAMINATION OF NERVOUS SYSTEM

A. SENSORY SYSTEM

a. Touch:

Perception: ☐

0 - Normal

1 - Decreased sensation

2 - Increased sensation

3 - Altered sensation

Area affected: ☐

1 - tips of fingers / toes

2 - Entire finger / toes

3 - Mid foot / hand

4 - Ankle / wrist

5 - Lower 1/3rd leg

6. Upper 2/3rd leg

b. Pain: ☐

N – Not affected

Y – Affected

Area affected ☐

1 - tips of fingers / toes

2 - Entire finger / toes

3 - Mid foot / hand

4 - Ankle / wrist

5 - Lower 1/3rd leg

6. Upper 2/3rd leg

c). Position sense : ☐

N- Not affected

Y-Affected

B. MOTOR SYSTEM

1. Nutrition : ☐

1 - Normal

2 – Wasting

2. Power : Grade ☐

1. No movement
2. Flickering movement
3. Present but not against gravity
4. Present against gravity but reduced
5. Normal

3. Reflexes : ☐

AUDIOLOGICAL EXAMINATION

1. Examination of the external auditory meatus

2. Examination of the tympanic membrane

3) Tuning fork tests :

a) Rinne test :----------

b) Weber test : ----------

c) Absolute bone conduction test : ----------

4) Pure tone audiometry :

Right ear : ----------

Left ear : ----------

ANNEXURE - III

CONSENT FORM

I Ms./Mrs./Mr.---------- understand that Dr.xxxxxxxxx, a Postgraduate student in Madras Medical College, Chennai is doing this study on "evaluation of nerve conduction abnormalities and brainstem auditory evoked potential in Type 2 Diabetes Mellitus". I have been explained about the study in details. These tests are simple, involve the recording of evoked potential after giving visual stimulus. Nerve conduction study involves stimulation of the nerve by a very minimal current which is absolutely harmless. They do not involve injections or taking any medicines and are risk free. I am participating in this study willingly .I have not been forced to do so. I have also been told clearly that I could withdraw from this study without any prejudice.

YOURS TRULY

(Signature of the subject)

Name : _____

Date and Time : _____

(TO BE FILLED BY THE SUBJECT AND PATIENTS)

(SIGNATURE OF RESEARCHER)

Nerve conduction study of median nerve (sensory and motor) and tibial nerve (motor) in diabetic group.
DD – diabetes duration , LAT –latency, AMP – amplitude and NCV – nerve conduction velocity.

S.NO	AGE	SEX	HT	WT	BMI	DD	MEDIAM NERVE SENSORY DIVISION			MEDIAN NERVE MOTOE DIVISION			TIBIAL NERVE		
							LAT(ms)	AMP(µv)	NCV((m/s)	LAT(ms)	AMP(mv)	NCV((m/s)	LAT(ms)	AMP(mv)	NCV(m/s)
1	45	M	165	74	27.18	4	4.26	18.5	45.86	5.39	2.4	44.74	6.94	3.2	41.52
2	48	M	168	72	25.51	6	4.18	19.7	44.36	6.37	3.1	45.04	7.02	2.8	37.55
3	37	F	155	68	28.30	5	4.58	16.3	48.16	5.25	2.8	46.76	8.15	2.9	39.62
4	38	M	165	65	23.87	3	4.76	19.3	50.34	4.28	2.6	48.64	7.14	3.4	37.16
5	42	M	166	62	22.49	2	4.86	20.8	44.68	5.17	2.7	46.24	6.88	2.6	34.56
6	53	F	150	55	24.44	4	4.64	20.2	47.04	6.9	3	48.86	8.26	3	36.52
7	42	M	168	73	25.86	5	5.28	15.7	46.64	5.62	4.4	50.06	7.22	2.7	40.03
8	46	M	172	70	23.66	3	4.13	24.9	44.48	3.92	4.5	51.24	7.82	2.4	38.86
9	52	F	164	60	22.30	6	2.93	27.3	46.36	3.66	4.9	42.55	7.96	3.6	36.64
10	45	M	165	70	25.71	7	3.06	24.5	50.42	3.48	5.2	56.06	6.93	3.8	38.18
11	46	F	160	65	25.39	5	2.83	28.3	52.82	3.76	5.3	54.86	4.38	4	37.01
12	48	M	168	72	25.51	3	3.37	26.7	54.38	3.86	4.5	55.12	5.44	4.0	44.44
13	50	F	162	66	25.14	7	3.15	28.5	54.06	3.23	4.7	57.14	5.04	4.5	46.54
14	47	M	166	72	26.12	2	3.08	23.6	51.16	3.4	4.6	55.27	4.77	4.5	44.36
15	39	F	155	64	26.63	3	3.64	24.6	50.82	3.21	4.8	54.78	4.56	4.4	45.12
16	36	M	164	69	25.65	1	2.9	25.6	52.65	2.73	4.4	55.12	5.13	3.7	45.65
17	41	M	172	78	26.36	4	2.58	26.3	51.06	3.33	4.5	56.25	5.3	4.1	45.05
18	43	F	158	64	25.63	5	3.43	32.5	51.75	3.18	4.5	54.92	5.72	4	45.22
19	45	F	155	62	25.80	3	3.66	25.2	52.02	3.15	4.1	54.88	5.46	3.8	43.84
20	37	M	165	74	27.18	1	2.92	25.4	53.34	2.85	4	55.34	4.96	4.2	44.36

Nerve conduction study of median nerve (sensory and motor) and tibial nerve (motor) in diabetic group.

DD – diabetes duration , LAT –latency, AMP – amplitude and NCV – nerve conduction velocity.

S.NO	AGE	SEX	HT	WT	BMI	DD	MEDIAM NERVE SENSORY DIVISION			MEDIAN NERVE MOTOE DIVISION			TIBIAL NERVE		
							LAT(ms)	AMP(µv)	NCV(m/s)	LAT(ms)	AMP(mv)	NCV((m/s)	LAT(ms)	AMP(mv)	NCV(m/s)
21	55	M	16	75	27.54	14	4.49	19.6	48.24	6.12	2.2	44.36	7.56	2.4	35.01
22	53	M	16	73	26.17	13	5.53	18.4	42.33	4.97	2.7	45.63	8.34	3	36.26
23	54	F	15	69	29.09	11	4.13	16.6	42.53	4.96	1.8	46.74	8.22	3.1	36.07
24	54	F	16	66	24.53	13	4.27	15.1	44.53	6.4	2.3	46.8	7.23	2.8	36.62
25	55	M	16	63	23.14	15	4.91	17.3	44.34	4.75	2.4	45.16	8.76	2.9	35.75
26	55	M	14	56	25.56	15	5.73	16.7	44.18	6.94	1.9	47.35	6.54	3	37.01
27	50	M	16	74	26.85	9	4.85	15.6	50.2	4.83	2	44.66	7.54	2.6	37.1
28	54	M	17	71	24.56	15	5.82	15.6	46.14	6.62	2.2	45.62	6.37	2.7	35.73
29	52	F	16	61	23.24	13	4.16	17.8	43.35	4.26	2.3	45.06	7.16	2.9	36.16
30	49	M	16	71	26.72	10	5.84	18.6	45.14	5.36	3.3	44.12	7.34	2.9	35.16
31	47	F	15	66	26.43	11	4.65	15.2	43.24	6.15	3	45.16	8.16	2.5	38.72
32	48	M	16	74	26.85	10	5.04	25.4	43.96	6.16	5	46.24	7.88	3	35.22
33	50	M	16	68	26.56	11	5.96	23.8	46.34	4.72	4.4	44.88	8.76	3.6	37.23
34	47	M	16	74	26.53	9	4.72	24.3	43.92	6.48	4.2	44.16	7.34	3.8	39.01
35	47	F	15	66	27.12	9	4.96	23.8	44.42	4.56	4.3	55.68	8.15	3.8	38.18
36	45	F	16	68	24.97	11	3.23	24.5	44.94	4.1	4.7	55.82	8.06	3.9	35.18
37	44	M	17	77	25.72	8	3.08	23.5	51.76	3.17	4.3	55.16	5.37	4.1	36.15
38	46	F	15	63	24.91	9	3.26	23.6	52.24	3.76	4.5	56.78	5.72	3.6	43.96
39	45	F	15	61	25.06	10	3.42	24.7	51.26	3.3	4.9	55.38	4.98	3.6	45.66
40	47	M	16	73	26.49	10	3.5	27.2	51.65	2.71	4.2	55.92	5.06	3.7	44.78

Nerve conduction study of media n nerve (sensory and motor), and tibial nerve (motor) in control group.

S.NO	AGE	SEX	HT	WT	BMI	MEDIAM NERVE SENSORY DIVISION			MEDIAN NERVE MOTOE DIVISION			TIBIAL NERVE		
						LAT(ms)	AMP(µv)	NCV(m/s)	LAT(ms)	AMP(µv)	NCV(m/s)	LAT(ms)	AMP(µv)	NCV(m/s)
1	45	M	160	72	28.12	2.67	28.8	61.42	3.4	6.1	59.38	5.44	4.4	46.56
2	38	M	158	66	26.43	4.3	35.2	59.43	2.37	7.5	56.74	4.38	4.6	47.46
3	42	M	165	70	25.71	3.1	37.6	61.02	3.14	8.6	57.58	5.62	4.8	46
4	46	F	158	60	24.03	3.22	34.8	57.15	3.65	7.2	57.01	4.47	4	47.2
5	47	M	170	72	24.91	2.57	38.6	53.82	2.96	9	59.12	5.5	4.5	46.9
6	38	F	162	58	22.10	2.98	37	52.9	3.24	9.3	54.08	4.76	4.7	47.3
7	41	M	168	64	22.67	3.19	38.8	57.52	3.53	6.9	57.62	4.82	4.5	46.11
8	42	M	176	75	24.21	3.12	30.8	55.28	3.48	9.4	56.33	4.93	3.6	48.18
9	45	M	170	78	26.98	3.88	27.4	58.88	3.55	9.2	58.24	4.98	3.6	45.72
10	36	F	165	65	23.87	2.9	30.4	57.78	3.7	7	56.98	5.12	4.1	47.02
11	38	F	165	65	23.87	3.06	34.7	54.96	3.59	6.5	57.03	5.26	4.3	46.58
12	40	F	160	64	25	3.04	35.7	55.23	3.82	9.4	60.13	5.38	3.9	48.59
13	46	M	168	72	25.51	3.14	36.7	60.88	3.63	9.4	56.14	5.66	3.7	47.42
14	42	M	170	71	24.56	3	37.4	54.32	3.45	9.6	54.34	5.76	3.8	45.2
15	35	M	165	68	24.97	2.76	31.9	57.54	3.75	9.2	57.63	5.78	4.4	46.44
16	37	M	168	78	27.63	2.98	31.3	51.84	3.6	8.3	50.14	5.8	4.8	48.42
17	42	M	160	74	28.90	2.74	32	58.26	3.61	8.3	60.16	4.34	4.7	46.64
18	39	M	158	70	28.04	2.98	33.2	54.2	3.51	7.7	54.38	4.46	4.5	47.58
19	42	F	155	65	27.05	3.23	28.4	51.36	3.46	7.7	58.16	4.72	4.1	46.36
20	43	F	153	62	26.48	2.97	32	56.04	3.58	5.5	55.63	4.88	4	48.56

Nerve conduction study of media n nerve (sensory and motor), and tibial nerve (motor) in control group.

S.NO	AGE	SEX	HT	WT	BMI	MEDIAM NERVE SENSORY DIVISION			MEDIAN NERVE MOTOE DIVISION			TIBIAL NERVE		
						LAT(ms)	AMP(µv)	NCV(m/s)	LAT(ms)	AMP(µv)	NCV(m/s)	LAT(ms)	AMP(µv)	NCV(m/s)
21	51	F	160	65	25.39	2.63	32.3	51.16	3.54	9	58.88	4.94	4.5	47.6
22	42	M	170	74	25.60	3.23	31.1	55.06	3.43	8.4	59.64	4.92	4.7	46.68
23	44	M	168	70	24.80	3.17	29.3	54.12	3.48	6.8	57.47	5.54	4.7	48.52
24	45	F	150	58	25.77	3.06	33.8	54.37	3.86	6.2	58.02	5.72	4.3	48.14
25	36	M	162	68	25.91	3.01	38.1	55.31	4	6.9	55.12	5.5	3.9	46.26
26	40	F	155	68	28.30	2.83	36.5	57.32	3.57	8.6	56.77	4.5	4	46.53
27	39	M	165	70	25.71	3.18	31.8	57.76	3.59	7.4	58.15	4.53	4.5	49.78
28	41	M	160	72	28.12	3.14	29.4	56.72	4.08	7.1	56.31	4.59	4.1	46.23
29	45	F	160	70	27.34	3.6	38.6	50.77	3.54	8.6	50.36	4.3	4.2	47.36
30	43	M	168	82	29.05	2.9	38.1	54.79	3.7	6.1	58.18	4.27	3.8	46.79
31	37	M	170	78	26.98	2.88	38.8	54.78	3.61	5.7	57.13	4.13	3.9	48.39
32	36	F	155	68	28.30	2.78	29.8	56.54	3.52	8.9	58.16	5.72	4.1	48.08
33	44	F	150	65	28.88	3.12	30.2	52.86	3.8	6.3	57.04	5.65	4.1	48.15
34	50	F	160	55	21.48	2.8	38.2	48.72	3.46	5.8	52.48	6.68	3.6	44.65
35	43	M	165	56	20.56	2.61	39.3	52.04	3.6	6.7	57.28	5.4	4.1	46.66
36	46	M	168	76	26.92	3	30.2	53.34	3.8	7.3	59.19	5.32	5	48.44
37	42	F	152	55	23.80	2.89	32.4	49.26	3.92	7.4	57.14	5.26	4.5	48.62
38	39	F	155	60	24.97	2.68	33.2	55.32	3.88	8.4	57.73	5.17	4.5	49.21
39	40	M	168	63	22.32	2.92	29.8	53.44	3.6	8.1	58.13	5.2	3.9	46.61
40	42	M	165	71	26.07	2.75	44.8	54.98	3.57	9.3	60.46	5.22	4	47.58

Brainstem auditory evoked potential latencies in diabetic group – RIGHT EAR

S.NO	AGE	SEX	HT	WT	BMI	DD	BAEP LATENCY –RIGHT EAR (ms)							
							I	II	III	IV	V	I-III	I-V	III-V
1	45	M	165	74	27.18	4	1.46	2.73	3.9	4.98	6.4	2.44	4.94	2.5
2	48	M	168	72	25.51	6	1.48	2.63	3.98	4.98	6.42	2.5	4.94	2.44
3	37	F	155	68	28.30	5	1.48	2.56	4.02	4.86	6.5	2.54	5.02	2.48
4	38	M	165	65	23.87	3	1.5	2.65	3.98	4.9	6.52	2.48	5.02	2.54
5	42	M	166	62	22.49	2	1.42	2.72	3.96	4.8	6.42	2.54	5	2.46
6	53	F	150	55	24.44	4	1.42	2.5	4	4.92	6.46	2.58	5.04	2.46
7	42	M	168	73	25.86	5	1.52	2.5	3.98	4.82	6.4	2.46	4.88	2.42
8	46	M	172	70	23.66	3	1.55	2.8	3.83	4.94	6.53	2.28	4.98	2.7
9	52	F	164	60	22.30	6	1.56	2.7	3.54	5.02	5.86	1.98	4.3	2.32
10	45	M	165	70	25.71	7	1.6	2.86	3.7	5.08	5.8	2.1	4.2	2.1
11	46	F	160	65	25.39	5	1.54	2.75	3.75	4.9	5.77	2.21	4.23	2.02
12	48	M	168	72	25.51	3	1.52	2.68	3.55	4.96	5.8	2.03	4.28	2.25
13	50	F	162	66	25.14	7	1.44	2.68	3.6	5.1	5.76	2.16	4.32	2.16
14	47	M	166	72	26.12	2	1.52	2.8	3.65	5.02	5.94	2.13	4.42	2.29
15	39	F	155	64	26.63	3	1.5	2.85	3.7	5.06	5.85	2.2	4.35	2.15
16	36	M	164	69	25.65	1	1.48	2.75	3.74	4.76	5.86	2.26	4.38	2.12
17	41	M	172	78	26.36	4	1.52	2.76	3.81	4.85	5.92	2.29	4.4	2.11
18	43	F	158	64	25.63	5	1.57	2.78	3.55	4.94	5.84	1.98	4.27	2.29
19	45	F	155	62	25.80	3	1.52	2.7	3.62	5.02	5.86	2.1	4.34	2.24
20	37	M	165	74	27.18	1	1.58	2.82	3.72	5.06	5.78	2.14	4.2	2.06

Brainstem auditory evoked potential latencies in diabetic group – RIGHT EAR.

S.NO	AGE	SEX	HT	WT	BMI	DD	BAEP LATENCY –RIGHT EAR (ms)							
							I	II	III	IV	V	I-III	I-V	III-V
21	55	M	165	75	27.54	14	1.46	2.65	3.88	5.08	6.5	2.42	5.04	2.62
22	53	M	167	73	26.17	13	1.44	2.68	3.86	5.06	6.74	2.42	5.3	2.88
23	54	F	154	69	29.09	11	1.5	2.68	3.94	5.04	6.81	2.44	5.31	2.87
24	54	F	164	66	24.53	13	1.44	2.71	3.9	4.92	6.76	2.46	5.32	2.86
25	55	M	165	63	23.14	15	1.44	2.66	3.84	4.82	6.77	2.4	5.33	2.93
26	55	M	148	56	25.56	15	1.43	2.72	3.88	4.9	6.74	2.45	5.31	2.86
27	50	M	166	74	26.85	9	1.4	2.6	3.82	4.9	6.7	2.42	5.3	2.88
28	54	M	170	71	24.56	15	1.42	2.74	3.9	4.82	6.78	2.48	5.36	2.88
29	52	F	162	61	23.24	13	1.48	2.62	3.92	4.76	6.76	2.44	5.28	2.84
30	49	M	163	71	26.72	10	1.46	2.74	3.94	4.82	6.8	2.48	5.34	2.86
31	47	F	158	66	26.43	11	1.42	2.94	3.84	5.06	6.78	2.42	5.36	2.94
32	48	M	166	74	26.85	10	1.44	2.82	3.88	5.08	6.8	2.44	5.36	2.92
33	50	M	160	68	26.56	11	1.52	3.08	3.96	5.08	6.4	2.44	4.88	2.44
34	47	M	167	74	26.53	9	1.56	2.77	3.77	4.92	6.51	2.21	4.95	2.74
35	47	F	156	66	27.12	9	1.54	2.7	3.53	4.94	5.7	1.99	4.16	2.17
36	45	F	165	68	24.97	11	1.46	2.7	3.58	5.12	5.65	2.12	4.19	2.07
37	44	M	173	77	25.72	8	1.56	2.84	3.67	5.04	5.75	2.11	4.19	2.08
38	46	F	159	63	24.91	9	1.54	2.85	3.7	5.08	5.78	2.16	4.24	2.08
39	45	F	156	61	25.06	10	1.52	2.77	3.72	4.76	5.84	2.2	4.32	2.12
40	47	M	166	73	26.49	10	1.56	2.76	3.76	4.84	5.72	2.2	4.16	1.96

Brainstem auditory evoked potential latencies in diabetic group – LEFT EAR.

S.NO	AGE	SEX	HT	WT	BMI	DD	BAEP LATENCY –RIGHT EAR (ms)							
							I	II	III	IV	V	I-III	I-V	III-V
1	45	M	165	74	27.18	4	1.48	2.6	3.92	5.06	6.42	2.44	4.94	2.5
2	48	M	168	72	25.51	6	1.42	2.68	3.96	5.02	6.44	2.54	5.02	2.48
3	37	F	155	68	28.30	5	1.46	2.67	4	4.76	6.52	2.54	5.06	2.52
4	38	M	165	65	23.87	3	1.48	2.74	4.02	4.98	6.5	2.54	5.02	2.48
5	42	M	166	62	22.49	2	1.46	2.8	3.98	4.86	6.44	2.52	4.98	2.46
6	53	F	150	55	24.44	4	1.42	2.58	3.96	4.92	6.48	2.54	5.06	2.52
7	42	M	168	73	25.86	5	1.44	2.5	4	4.88	6.42	2.56	4.98	2.42
8	46	M	172	70	23.66	3	1.52	2.88	4	4.94	6.43	2.48	4.91	2.43
9	52	F	164	60	22.30	6	1.58	2.76	3.68	5.04	5.88	2.1	4.3	2.2
10	45	M	165	70	25.71	7	1.54	2.88	3.64	5.14	5.8	2.1	4.26	2.16
11	46	F	160	65	25.39	5	1.6	2.78	3.73	4.96	5.7	2.13	4.1	1.97
12	48	M	168	72	25.51	3	1.54	2.68	3.55	4.98	5.7	2.01	4.16	2.15
13	50	F	162	66	25.14	7	1.53	2.78	3.6	5.14	5.72	2.07	4.19	2.12
14	47	M	166	72	26.12	2	1.48	2.9	3.69	5.06	5.77	2.21	4.29	2.08
15	39	F	155	64	26.63	3	1.58	2.92	3.7	5.12	5.8	2.12	4.22	2.1
16	36	M	164	69	25.65	1	1.58	2.82	3.72	4.74	5.86	2.14	4.28	2.14
17	41	M	172	78	26.36	4	1.59	2.76	3.78	4.88	5.74	2.19	4.15	1.96
18	43	F	158	64	25.63	5	1.5	2.8	3.8	4.94	5.78	2.3	4.28	1.98
19	45	F	155	62	25.80	3	1.62	2.7	3.56	5.04	5.86	1.94	4.24	2.3
20	37	M	165	74	27.18	1	1.54	2.9	3.66	5.12	5.76	2.12	4.22	2.1

Brainstem auditory evoked potential latencies in diabetic group – LEFT EAR.

S.NO	AGE	SEX	HT	WT	BMI	DD	BAEP LATENCY –RIGHT EAR (ms)							
							I	II	III	IV	V	I-III	I-V	III-V
21	55	M	165	75	27.54	14	1.44	2.66	3.88	5.14	6.52	2.44	5.08	2.64
22	53	M	167	73	26.17	13	1.42	2.7	3.86	5.14	6.76	2.44	5.34	2.9
23	54	F	154	69	29.09	11	1.44	2.68	3.9	5.04	6.84	2.46	5.4	2.94
24	54	F	164	66	24.53	13	1.42	2.74	3.88	4.96	6.8	2.46	5.38	2.92
25	55	M	165	63	23.14	15	1.46	2.7	3.92	4.84	6.82	2.46	5.36	2.9
26	55	M	148	56	25.56	15	1.45	2.68	3.9	4.86	6.78	2.45	5.33	2.88
27	50	M	166	74	26.85	9	1.52	2.6	3.84	4.84	6.76	2.32	5.24	2.92
28	54	M	170	71	24.56	15	1.46	2.8	3.89	4.8	6.8	2.43	5.34	2.91
29	52	F	162	61	23.24	13	1.56	2.62	3.98	4.76	6.82	2.42	5.26	2.84
30	49	M	163	71	26.72	10	1.52	2.72	3.98	4.82	6.86	2.46	5.34	2.88
31	47	F	158	66	26.43	11	1.42	2.94	3.86	5.16	6.8	2.44	5.38	2.94
32	48	M	166	74	26.85	10	1.42	2.94	3.9	5.14	6.78	2.48	5.36	2.88
33	50	M	160	68	26.56	11	1.42	3.08	3.94	5.06	6.42	2.52	5	2.48
34	47	M	167	74	26.53	9	1.48	2.75	3.92	4.98	6.6	2.44	5.12	2.68
35	47	F	156	66	27.12	9	1.56	2.66	3.55	5	5.74	1.99	4.18	2.19
36	45	F	165	68	24.97	11	1.49	2.74	3.71	5.1	5.82	2.22	4.33	2.11
37	44	M	173	77	25.72	8	1.6	2.84	3.68	5.04	5.86	2.08	4.26	2.18
38	46	F	159	63	24.91	9	1.54	2.91	3.72	5.1	5.85	2.18	4.31	2.13
39	45	F	156	61	25.06	10	1.52	2.8	2.78	4.78	5.9	1.26	4.38	3.12
40	47	M	166	73	26.49	10	1.55	2.84	3.81	4.88	5.82	2.26	4.27	2.01

Brainstem auditory evoked potential latencies in control group

S.NO	BAEP LATENCIES –RIGHT EAR								BAEP LATENCIES –LEFT EAR							
	I	II	III	IV	V	I-III	I-V	III-V	I	II	III	IV	V	I-III	I-V	III-V
1	1.46	2.76	3.68	5.04	5.82	2.22	4.36	2.14	1.48	2.8	3.7	5.02	5.86	2.22	4.38	2.16
2	1.44	2.8	3.7	5.08	5.76	2.26	4.32	2.06	1.46	2.8	3.74	5.04	5.78	2.28	4.32	2.04
3	1.5	2.78	3.66	5.02	5.6	2.16	4.1	1.94	1.51	2.82	3.66	5.04	5.6	2.15	4.09	1.94
4	1.44	2.82	3.62	4.94	5.66	2.18	4.22	2.04	1.44	2.78	3.65	4.96	5.65	2.21	4.21	2
5	1.44	2.8	3.54	4.86	5.75	2.1	4.31	2.21	1.44	2.84	3.54	4.9	5.75	2.1	4.31	2.21
6	1.43	2.76	3.56	4.9	5.8	2.13	4.37	2.24	1.46	2.8	3.58	4.92	5.82	2.12	4.36	2.24
7	1.4	2.7	3.6	4.92	5.68	2.2	4.28	2.08	1.42	2.72	3.62	4.88	5.7	2.2	4.28	2.08
8	1.42	2.84	3.48	4.88	5.72	2.06	4.3	2.24	1.44	2.82	3.54	4.9	5.74	2.1	4.3	2.2
9	1.48	2.78	3.58	4.8	5.7	2.1	4.22	2.12	1.46	2.82	3.58	4.82	5.72	2.12	4.26	2.14
10	1.46	2.8	3.6	4.9	5.7	2.14	4.24	2.1	1.46	2.84	3.62	4.92	5.74	2.16	4.28	2.12
11	1.42	3	3.58	5	5.62	2.16	4.2	2.04	1.42	2.96	3.6	5.02	5.62	2.18	4.2	2.02
12	1.44	2.9	3.54	5.02	5.66	2.1	4.22	2.12	1.42	2.93	3.58	5	5.66	2.16	4.24	2.08
13	1.45	3.02	3.46	5	5.74	2.01	4.29	2.28	1.46	2	3.48	5.02	5.78	2.02	4.32	2.3
14	1.46	2.7	3.56	4.94	5.85	2.1	4.39	2.29	1.46	2.99	3.55	4.96	5.9	2.09	4.44	2.35
15	1.48	2.68	3.52	4.96	5.52	2.04	4.04	2	1.5	2.7	3.54	4.98	5.54	2.04	4.04	2
16	1.5	2.6	3.48	4.86	5.7	1.98	4.2	2.22	1.5	2.64	3.5	4.9	5.7	2	4.2	2.2
17	1.5	2.65	3.62	4.9	5.6	2.12	4.1	1.98	1.5	2.66	3.62	4.92	5.62	2.12	4.12	2
18	1.42	2.76	3.68	4.8	5.65	2.26	4.23	1.97	1.4	2.76	3.7	4.8	5.66	2.3	4.26	1.96
19	1.42	2.56	3.55	4.94	5.64	2.13	4.22	2.09	1.42	2.56	3.55	4.92	5.64	2.13	4.22	2.09
20	1.52	2.58	3.56	4.84	5.68	2.04	4.16	2.12	1.54	2.6	3.56	4.84	5.7	2.02	4.16	2.14

Brainstem auditory evoked potential latencies in control group

S.NO	BAEP LATENCIES –RIGHT EAR								BAEP LATENCIES –LEFT EAR							
	I	II	III	IV	V	I-III	I-V	III-V	I	II	III	IV	V	I-III	I-V	III-V
21	1.56	2.7	3.6	4.92	5.64	2.04	4.08	2.04	1.53	2.7	3.58	4.9	5.62	2.05	4.09	2.04
22	1.54	2.78	3.58	4.96	5.72	2.04	4.18	2.14	1.54	2.76	3.6	4.98	5.72	2.06	4.18	2.12
23	1.46	2.72	3.56	5.04	5.65	2.1	4.19	2.09	1.48	2.74	3.58	5	5.65	2.1	4.17	2.07
24	1.52	2.68	3.6	4.94	5.75	2.08	4.23	2.15	1.5	2.7	3.64	4.96	5.78	2.14	4.28	2.14
25	1.44	2.88	3.53	4.98	5.78	2.09	4.34	2.25	1.44	2.88	3.55	4.94	5.8	2.11	4.36	2.25
26	1.52	2.78	3.59	4.86	5.64	2.07	4.12	2.05	1.52	2.79	3.59	4.88	5.68	2.07	4.16	2.09
27	1.56	2.8	3.65	4.84	5.72	2.09	4.16	2.07	1.52	2.8	3.68	4.82	5.7	2.16	4.18	2.02
28	1.55	2.84	3.61	4.94	5.68	2.06	4.13	2.07	1.52	2.84	3.64	4.92	5.64	2.12	4.12	2
29	1.46	2.72	3.57	4.93	5.66	2.11	4.2	2.09	1.44	2.74	3.58	4.94	5.65	2.14	4.21	2.07
30	1.6	2.8	3.54	4.94	5.8	1.94	4.2	2.26	1.56	2.82	3.54	4.94	5.8	1.98	4.24	2.26
31	1.54	2.78	3.52	4.94	5.77	1.98	4.23	2.25	1.54	2.8	3.54	4.9	5.75	2	4.21	2.21
32	1.52	2.7	3.48	4.98	5.78	1.96	4.26	2.3	1.48	2.74	3.5	5.02	5.76	2.02	4.28	2.26
33	1.44	2.8	3.46	4.86	5.6	2.02	4.16	2.14	1.48	2.82	3.42	4.9	5.58	1.94	4.1	2.16
34	1.52	2.68	3.6	5.02	5.62	2.08	4.1	2.02	1.54	2.7	3.58	5.04	5.6	2.04	4.06	2.02
35	1.5	2.86	3.58	4.92	5.7	2.08	4.2	2.12	1.5	2.84	3.6	4.94	5.72	2.1	4.22	2.12
36	1.48	2.8	3.6	4.88	5.66	2.12	4.18	2.06	1.5	2.82	3.58	4.92	5.68	2.08	4.18	2.1
37	1.52	2.8	3.55	4.85	5.72	2.03	4.2	2.17	1.57	2.82	3.52	4.88	5.7	1.95	4.13	2.18
38	1.57	2.8	3.5	4.94	5.66	1.93	4.09	2.16	1.6	2.84	3.5	4.96	5.68	1.9	4.08	2.18
39	1.52	2.78	3.56	4.97	5.72	2.04	4.2	2.16	1.54	2.78	3.58	4.99	5.7	2.04	4.16	2.12
40	1.58	2.84	3.54	5.02	5.74	1.96	4.16	2.2	1.56	2.86	3.54	5.04	5.72	1.98	4.16	2.18